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SUPERFICIAL NONINVASIVE INTRAEPITHELIAL TUMORS OF THE CERVIX

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IN REVIEWING the reports on the early diagnosis of genital carcinoma, a significantly increasing number of early superficial epitheliomata of the cervix is noted.

Our interest in this problem has been stimulated recently by the occurrence, on our gynecologic service, of several early noninvasive epitheliomata of the cervix. With the problem of early diagnosis in mind, all the material on file of lesions of the cervix was carefully reviewed. In every instance in which the old microscopic slides revealed suspicious or interesting changes, the original blocks of tissue were recut. Often serial sections were made and in one instance the tissue was re-embedded in order to obtain better orientation of the tissue. The clinical records of these cases were also carefully studied.

From January, 1927, through April, 1943, four hundred and six primary squamous cell epitheliomata have been observed on the gynecologic service. Of these four hundred and six cases, seventeen were early, superficial lesions. In ten cases the diagnosis was made from the examination of curettings from grossly normal appearing cervixes in individuals with fibromyomata or chronic inflammatory disease of the adnexa. In only two cases were minute gross lesions of the cervix noted clinically and both were interpreted as papillary erosions. In two instances the disease had its origin in cervical polyps.

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Case Reports

Case 1.—Unit No. 78502. This case is presented in considerable detail because of its unusual interest.

The patient was first seen in October, 1927, because of irregular vaginal spotting. She was 55 years of age. She had had a supra-vaginal hysterectomy in 1910. Examination revealed a large, red, granular cervical polyp, protruding from the external os, which bled easily on manipulation. This was avulsed and the base was curetted.

Sloane Pathology No. 2457. Microscopic sections of tissue revealed an irregular, somewhat fragmented polypoid structure composed of delicate, rather edematous fibrous connective tissue. In several areas the surface was covered by a single layer of tall, cylindrical epithelium typical of the cervical mucosa. These cells appeared uniform in size and shape. The lining epithelium dipped into the subjacent stroma at irregular intervals to form numerous typical compound racemose glands, a few of which were dilated and cystic. The most striking feature of the lesion, however, was the presence of broad sheets of squamous epithelium which covered many portions of the surface of the polyp. Due to poor orientation of the tissue and obliquity of section, these bands of squamous cells appear in some regions to lie within the stroma. This is an artefact. These sheets of epithelium have no resemblance to the usual squamous metaplasia often seen in polyps. The cervical mucosa is often replaced by squamous cells, but invasion of the stroma is not seen.



Fig. 1.—(Case 1.) Low power view of cervical polyp showing extensive squamous metaplasia ($\times 5$).

These sheets of cells present a marked hypertrophy of the Malpighian zone. No evidence of stratification is present, the individual cells being piled one on another in a haphazard fashion. Acanthosis is minimal and everywhere the basement membrane is intact. The subepithelial stroma is quite vascular and slight to moderate infiltration of lymphocytes and plasma cells is noted. The basal cell layer appears relatively normal with the usual palisading pattern. However, the cells immediately above

this zone and extending up to the surface, present striking alterations. They have lost their normal orientation. They vary considerably in size, shape, and staining quality; nuclear patterns are variable. Two to four mitoses are seen in the high power fields. Deformed, bizarre, hyperchromatic nuclei, surrounded by clear spaces, are present. The individual cell outlines are indistinct, due to inter- and intracellular edema. Because of tangential section, a few round, or oval, plaques of these atypical squamous cells, seem to radiate around central clear spaces. (Figs. 1 and 2.)

Because of this interesting pattern, the original paraffin blocks were melted and the tissue was re-embedded, in an effort to acquire a more accurate orientation of the tissue. This met with only partial success.

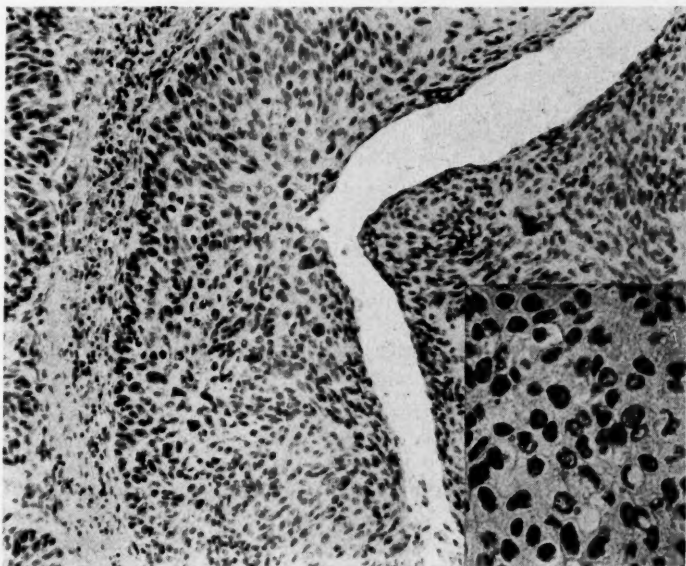


Fig. 2.—(Case 1.) High power view of polyp showing disorderly cellular arrangement in areas of metaplasia ($\times 150$). Insert reveals superficial resemblance to Bowen's disease ($\times 300$).

The patient remained well until January 16, 1929, when she was seen again because of a blood stained vaginal discharge of two months' duration. Examination under anesthesia revealed a somewhat contracted vaginal vault. The cervix was difficult to visualize. The mucosa presented a bright red, superficial, granular appearance. Bleeding occurred easily on manipulation. The tissues felt soft and pliable and presented none of the characteristics of epithelioma. On January 19, 1929, a biopsy of the cervix was done and scrapings from the granular surface were taken for examination.

Sloane Pathology No. 3192. Microscopic sections of cervical biopsy revealed a single ovoid plaque of dense fibrous tissue, one surface of which was covered by a band of squamous epithelium presenting all the characteristics of a noninvasive epithelioma. The scrapings from the vaginal vault revealed numerous strips of squamous epithelium, all showing the above described pattern.

The vaginal discharge continued. On March 11, 1930, cervical stump was noted to be small, atrophic, freely movable. The canal measured

2 cm. Posterior to the cervix was a bright red granular area which was divided by a ringlike contracture of vaginal mucosa. This tissue bled easily but did not feel thickened. Mucosa was soft and pliable. The tissue readily peeled off, like granulation tissue. One hundred milligrams of radium were left in this region for six hours. The lesion on the vaginal vault looked the same as before, except for lateral extension.

Sloane Pathology No. 4159. Microscopic sections of tissue revealed numerous broad strips of atypical squamous epithelial cells showing the same abnormal features described above.

On May 5, 1930, patient was given 400 mg. hours of radium. On October 8, 1930, it was noted that the patient was asymptomatic. The vaginal vault was occluded. On May 5, 1931, the patient had a sudden gush of fluid from vagina.

Examination on September 1, 1931, revealed a small opening in the occluded vaginal vault. On dilating this, the opening was found to lead to a small smooth lined cavity. No evidence of carcinoma noted. A biopsy was taken.

Sloane Pathology No. 5475. Microscopic section revealed a small piece of edematous connective tissue on which was superimposed a strip of squamous epithelium presenting changes from the normal as described above.

December 4, 1931, asymptomatic. No bleeding or discharge. Small opening in vaginal vault. May 13, 1933. Recurrence of serosanguineous discharge preceded by profuse vaginal bleeding. The constriction below the vault was firmer. No ulceration was seen.

October 5, 1933, biopsy of ring and scraping from vault were taken. The tissue lining the pocket was soft, pliable. Seventy-five mg.-hours of radium given. Sloane Pathology No. 7448. Microscopic sections of biopsy revealed the same type of squamous epithelium except that now slight invasion of subjacent stroma is noted. X-ray therapy was begun.

October, 1934, a recurrence of the vaginal discharge was noted. January 7, 1935, condition unaltered. Patient refused more radium.

April 11, 1935, biopsy of vault and 50 mg. of radium inserted for 49 hours. Sloane Pathology No. 9019 presents identical picture of previous biopsy.

When last heard from in 1938, the mild bladder and rectal symptoms, which were thought to be due to radium, were subsiding.

Case 2.—Unit No. 512001. A 65-year-old white gravida vii, whose menopause occurred twelve years previously, was first seen in March, 1937, because of vaginal bleeding for three months. Examination revealed a cervical polyp. At operation March 26, 1937, this structure, the cervix and adjacent vaginal mucosa revealed a superficial, bright red granular lesion which was easily removed with a curette, leaving a dull red moist surface. On April 13, 1937, patient received 70 mg. of radium for 100 hours. She was last seen in the follow-up clinic November 13, 1942, at which time patient was asymptomatic. The vaginal vault was contracted and the mucosa appeared normal.

Sloane Pathology No. 11130. Microscopic sections from curettings, from vagina, cervix, cervical canal revealed a similar pattern. Many irregular strips and plaques of abnormal stratified squamous epithelium were present, along with fragments of cervical mucosa and small fragments of fibromuscular tissue. The curettings from fundus consisted only of cervical epithelium showing squamous metaplasia or epidermi-

zation. All pieces of squamous epithelium, including scattered areas of squamous metaplasia from the polyp, showed uniformly abnormal changes, resembling an epithelioma. No pearl formation is seen anywhere. No involvement of the fibromuscular tissue was present and only the surface of the polyp was involved.

Case 3.—Unit No. 700876. A 50-year-old para ii, gravida vii, was admitted because of postmenopausal vaginal spotting of two years' duration. The menopause occurred six years ago. During the past two months she noted frequent episodes of bright red spotting.

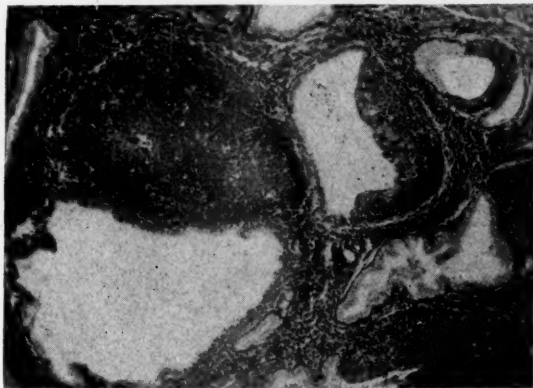


Fig. 3.—(Case 3.) Low power view of cervical biopsy showing extensive metaplasia ($\times 80$).

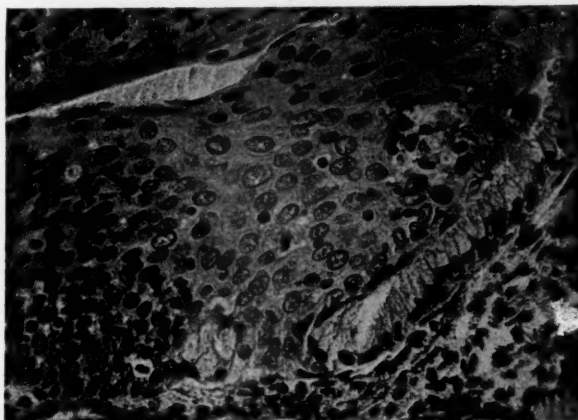


Fig. 4.—(Case 3.) High power view of details of metaplastic changes ($\times 200$).

Examination at time of curettage and biopsy of cervix on March 9, 1943, revealed a 3 mm. area just within the external os of the cervix which was granular, red, and presented small white papules, pinpoint in size. This area was excised in toto.

Sloane Pathology No. 18976 revealed marked squamous metaplasia of cervix with neoplastic alterations of the epithelium tending toward a Bowenoid pattern.

One week later, another biopsy was taken and radium inserted. The second biopsy failed to reveal any squamous epithelium. Apparently the entire lesion had been removed at the first operation.

The patient was given 6,000 mg.-hours of radium. (Figs. 3, 4 and 5.)

Case 4.—Unit No. 229808. A 53-year-old white woman was admitted because of intermittent vaginal spotting and watery discharge of two years' duration. Menopause occurred at 48 years of age.

On December 30, 1936, a curettage was done. Inspection of the cervix revealed an old deep laceration with one very small, slightly raised eroded area. A foul discharge was present.

Sloane Pathology No. 10867. The curettings from the fundus were normal. Tissue removed from the cervix with a curette revealed normal cervical mucosa with a dense stroma. In several areas the surface of the tissue was covered by atypical squamous epithelium and in one region a round plaque of squamous cells was seen just beneath the surface. Hyperplasia of the Malpighian zone was striking. The cells had lost their usual tendency toward stratification and varied moderately in size and shape. Mitoses were frequently noted.

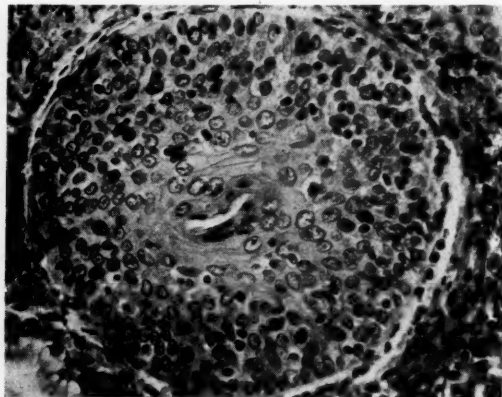


Fig. 5.—(Case 3.) High power view of cervical gland entirely replaced by squamous epithelium showing characteristic epitheliomatous changes ($\times 150$).

Patient was followed closely in the clinic where she was treated vigorously with estrogenic substances weekly, and douches because of senile vaginitis which manifested itself by a foul yellow vaginal discharge and occasional spotting.

She was last seen in May, 1931, and was asymptomatic. Her local condition had improved and no abnormalities were found on examination.

Case 5.—Unit No. 408675. The patient, aged 45, was admitted on November 3, 1939, because of metrorrhagia. In 1934, she had a curettage, amputation of cervix and repair of rectocele. The curettings revealed cystic glandular hyperplasia. Review of cervical tissue showed a superficial noninvasive epithelioma.

Sloane Pathology No. 8054. Microscopic sections of cervix revealed moderate squamous metaplasia involving some of the glands. The surface presented an area covered by abnormal squamous epithelium, revealing loss of stratification, disorientation of cells, 2 to 3 mitoses

per high power field, and moderate hyperplasia and hyperchromatic variable nuclei.

During 1938-1939, she received stilbestrol.

On examination on November 3, 1939, a small granular erosion of the cervix was noted. The cervix was biopsied.

Sloane Pathology No. 14267. Microscopic sections of tissue revealed strips of normal squamous epithelium, among which were several that presented hyperplasia, disorderly cellular arrangement, mitoses and nuclei varying markedly in size, shape and staining reaction.

On December 8, 1939, patient was readmitted and another biopsy was taken which showed only normal epithelium.

Patient was seen once in 1940, at which time she was asymptomatic and her physical findings locally were negative.

The entire lesion was apparently removed at the biopsy done on November 3, 1939.

Case 6.—Unit No. 280378. A 40-year-old colored woman, para v, gravida viii, was admitted on July 8, 1942, because of vaginal bleeding. On April 24, 1942, she had a curettage for incomplete abortion. Since then she has been spotting and her last period was quite profuse.

On July 10, 1942, a curettage was done. The cervix appeared eroded and a small 8 mm. fragment of tissue was removed. Sloane Pathology No. 18123. Microscopic sections of tissue revealed a small plaque of closely packed atypical squamous epithelial cells showing many mitoses.

On July 29, 1942, another biopsy was taken and 7,000 mg.-hours of radium given. Sloane Pathology No. 18188. Microscopic sections revealed no evidence of carcinoma in this second piece of cervical tissue. Apparently all disease had been removed.

March 19, 1943, no recurrence. No symptoms.

Case 7.—Unit No. 252697. A 28-year-old para i, gravida iii was admitted on November 28, 1939, because of abdominal pain, menorrhagia and metrorrhagia. She had a diagnostic curettage in 1931 for metrorrhagia. A normal endometrium was found.

A dilatation and curettage, and supravaginal hysterectomy were performed.

Sloane Pathology No. 14335. Among the curettings of normal endometrium were found several strips of stratified squamous epithelium revealing hyperplasia, loss of orientation of the individual cells, variation in size, shape and staining quality of the cells and their nuclei.

On January 10, 1940, a curettage and conization of the cervix was performed. Sloane Pathology No. 14472. Microscopic sections revealed abnormal squamous epithelium showing above-mentioned changes. (See Fig. 6.)

On February 7, 1940, patient was readmitted and given 2,700 mg.-hours of radium.

She was last seen on January 31, 1941, when she was asymptomatic and physical findings were negative.

Case 8.—Unit No. 367298. A 37-year-old colored para iii, gravida iii was admitted on January 21, 1933, because of abdominal pain of one year's duration and metrorrhagia for eight months. Examination revealed a badly lacerated and eroded cervix and a multinodular uterus the size of a three months' pregnancy.

A curettage, supravaginal hysterectomy, left salpingo-oophorectomy and right salpingectomy were performed.

Sloane Pathology No. 6786. Among the curettings were numerous broad strips of undifferentiated, atypical squamous epithelium. A few fragments of cervical glands were present showing metaplasia by a similar type of squamous epithelium.

Three weeks later the patient was given 5,000 mg.-hours of radium.

During 1934, 1935 and 1936, she received considerable x-ray therapy. Repeated follow-up examinations revealed a slowly progressive induration of the pelvis. She died in December, 1936.

Case 9.—Unit No. 691020. A 37-year-old white para vi, gravida vi was first seen in 1929 because of metrorrhagia for three months.

Examination revealed a firm, clean cervix and a slightly asymmetrically enlarged, firm uterus.

A curettage, supravaginal hysterectomy and perineorrhaphy were performed.

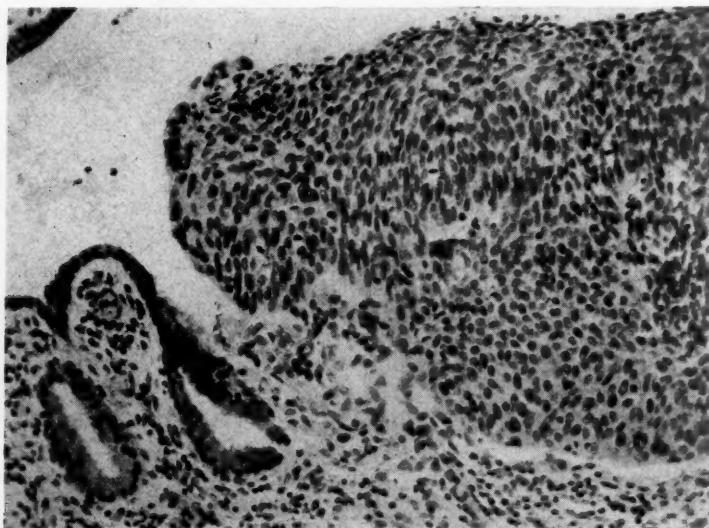


Fig. 6.—(Case 7.) Low power view of lesion showing epidermidization and superficial epithelioma ($\times 150$).

Sloane Pathology No. 3621. Microscopic sections of curettings revealed large pieces of fibromuscular tissue, scattered throughout which were round and oval strips of atypical squamous epithelium which had almost entirely replaced all the cervical glands. Portions of the surface of the tissue were covered by a similar atypical epithelium.

Three weeks later she was given 2,400 mg.-hours of radium and this was followed up by deep x-ray therapy. She was seen last in 1942, at which time she was well and free of recurrence or metastases.

Case 10.—Unit No. 601602. A 45-year-old white para o, gravida i, was first seen in March 1941, because of menorrhagia and intermenstrual spotting of six months' duration.

On March 7th a curettage, biopsy of cervix and supravaginal hysterectomy were performed. The cervix was found to be deeply lacerated and eroded. The uterus was multinodular and the size of a three and one-half months' pregnancy.

Sloane Pathology No. 16110. Microscopic sections of cervical biopsy revealed marked squamous metaplasia of the cervix, showing many atypical features and very superficial invasion of stroma.

On March 20th, the patient was given 4,000 mg.-hours of radium. Subsequently she has had considerable radiation therapy.

When seen in March, 1943, she was well without evidence of recurrence.

Case 11.—Unit No. 308859. The patient, a 49-year-old colored para ii, gravida ii, was first seen in December, 1940, because of backache and menorrhagia for six months. Examination revealed a normal appearing but lacerated cervix. The uterus was irregularly enlarged.

A curettage, supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed.

Sloane Pathology No. 15784. Sections of curettings revealed typical squamous metaplasia of the cervix with definite epitheliomatous alterations both in cell pattern and the individual cells.

Six weeks later the patient was readmitted. The cervix appeared normal. A biopsy was taken and 4,000 mg.-hours of radium were given.

Sloane Pathology No. 16003 revealed a typical squamous cell epithelioma involving the cervical glands and resembling the previous curettings.

Subsequently this patient has received considerable deep x-ray therapy.

She was last seen in January, 1943, feeling well and free of local recurrences.

Case 12.—Unit No. 621585. The patient, a 42-year-old white para o, gravida ii was admitted for operation because of menorrhagia. Examination revealed a multinodular fibroid uterus the size of a four months' pregnancy. Grossly, the cervix appeared normal.

On September 10, 1940, a curettage, amputation of the cervix, supravaginal hysterectomy and left salpingo-oophorectomy were performed.

Sloane Pathology No. 15459. Among the curettings were numerous large strips of very atypical squamous epithelium. Sections of the cervix revealed extensive squamous metaplasia showing epitheliomatous changes.

One week later, the patient was given 5,000 mg.-hours of radium.

To date she has remained well and is free of local recurrence or distant metastases.

Case 13.—Unit No. 371492. A 33-year-old colored para o, gravida o was first seen in April 1933, because of a lump in her abdomen, menorrhagia and dysmenorrhea, for one year. Examination revealed a large multinodular uterus the size of a four and one-half months' pregnancy. The cervix appeared normal.

On April 14, 1933, a curettage, supravaginal hysterectomy, excision of vaginal cyst were performed.

Sloane Pathology No. 6990. Among curettings were noted several strips of atypical squamous epithelium.

On May 2, 1933, a biopsy of the cervix was performed. Examination revealed a typical squamous cell carcinoma in areas of metaplasia.

On May 3, 1933, the patient received 5,000 mg.-hours of radium.

Following radiation therapy she developed a pelvic cellulitis and vesicovaginal fistula. This was repaired.

She was followed closely and, in all, three unsuccessful attempts to close the fistula were undertaken.

No evidence of local recurrence of the carcinoma was noted.

In September, 1942, the patient died at Harlem Hospital of "intestinal obstruction."

Case 14.—Unit No. 664265. A 46-year-old white woman, para 0, gravida ii, was admitted for menorrhagia of two years' duration.

On January 5, 1942, a curettage and excision of the cervix were performed.

Surgical Pathology No. 80798 revealed an abundant secretory endometrium. Among curettings were noted several large plaques of atypical squamous epithelium showing hyperplasia, hypertrophy, loss of orientation and stratification. Two to four mitoses were seen, per high power field. Variation in size, shape and staining quality of the cells and nuclei was frequently seen. The tissue from the cervix revealed a small plaque of intact surface epithelium showing the same changes without any tendency toward invasion. This was considered by Dr. A. P. Stout to be a Bowenoid type of superficial epithelioma.



Fig. 7.—(Case 15.) Low power view of cervix. At left is seen the normal epithelium of the portio. The cervical canal is entirely lined by squamous epithelium. In the middle of the picture the epithelium alters abruptly and becomes transformed into a superficial epithelioma seen on the right ($\times 70$).

On April 8, 1942, a biopsy was taken and 5,000 mg.-hours of radium given.

Sloane Pathology No. 17746 revealed surface epithelium of portio vaginalis showing above described changes.

January 14, 1943 follow-up. Ocluded vault of vagina. No symptoms. No evidence of recurrence.

Case 15.—Unit No. 702514. A 38-year-old colored para i, gravida iii was first seen in April, 1943, because of enlarging abdominal mass of two and one-half years' duration. For the last year, there were periods of profuse bleeding every 2 to 4 weeks. Examination revealed a grossly normal cervix and a multinodular uterus the size of a three and one-half to four months' pregnancy.

On April 6, 1943, a complete hysterectomy and bilateral salpingo-oophorectomy were performed.

Sloane Pathology No. 19070. The uterus, tubes and ovaries were not remarkable. Grossly the cervix appeared normal. However, on examination of the microscopic sections the normal squamous epithelium of the portio vaginalis was found to extend up into the cervical canal for its entire length, replacing the columnar epithelium entirely. A distinct change in the epithelium had occurred. The notable changes included loss of stratification and orientation of the cells, with variation in cell and nuclear size, shape and staining qualities. Narrow tongues of epithelium dip deeply into the stroma. In one area, abnormal squamous cells lie free, close to the surface. Early pearl formation is seen in one area. Serial sections of the entire cervix revealed the same lesion throughout the tissues, with practically no invasion.

The patient will be given deep x-ray therapy. (Figs. 7 and 8.)

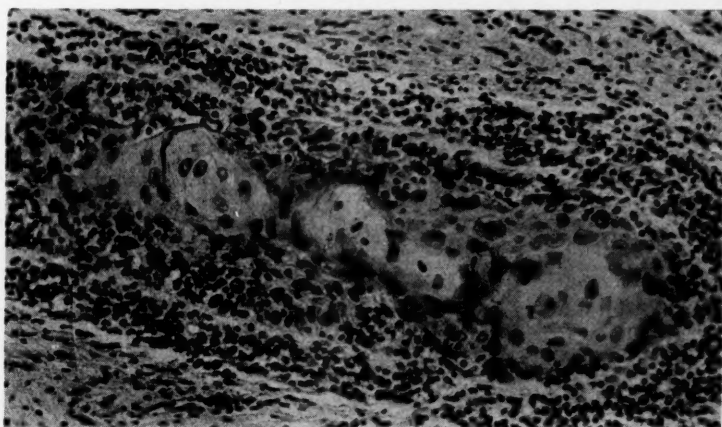


Fig. 8.—(Case 15.) High power view of portion of tongue of atypical squamous epithelium seen in Fig. 8 at right, dipping deeply into the stroma ($\times 300$).

Case 16.—Unit No. 705653. A 45-year-old white nullipara was first seen in April, 1943, because of menorrhagia and slight metrorrhagia. Examination revealed no abnormalities.

A curettage was performed. The curettings from the cervix were unusually abundant. For this reason 50 mg. of radium was inserted.

Sloane Pathology No. 19047. Cervical curettings revealed abundant tissue composed of cervical glands showing marked metaplasia. In several discrete isolated areas atypical squamous epithelium lay in between the glands in the stroma, and early pearl formation was seen. Squamous metaplasia, of an atypical type, was prominent. The endometrium was hyperplastic and showed some cystic changes.

The patient received 6,000 mg.-hours of radium.

Case 17.—Unit No. 707686. A 43-year-old colored para ii, gravida iii was first seen in March, 1943, because of enlarging abdominal mass for two years. Except for one recent episode of menorrhagia, she has had no abnormal bleeding. Examination revealed a lacerated infected cervix and a large multinodular uterus the size of a five months' pregnancy.

On March 30, 1943, a curettage, complete abdominal hysterectomy and bilateral salpingo-oophorectomy were performed.

Sloane Pathology No. 19042. The curettings were abundant. On microscopic examination the tissue was seen to be composed almost entirely of cervical glands, revealing striking squamous metaplasia which appeared frequently very atypical, with many abnormal cells and early pearl formations. The cervical glands were rather hyperplastic. Serial sections of the cervix revealed that almost all the mucosa had been removed with the curette. Only in one or two areas were there noted, on the surface, small nests of squamous epithelium. The lining epithelium of the portio was normal. About midway up the cervical canal, was found a single localized patch of atypical epithelium dipping deeply into the stroma. Nearby were several small nests of atypical squamous epithelium lying in the connective tissue stroma. The histopathology of this case bears a marked resemblance to Case 15.

The patient will receive deep x-ray therapy.

Discussion

Of the seventeen cases of early superficial epitheliomas of the cervix, the average age incidence was 44.1 years. Symptoms covered a span of three months to two and one-half years, the average duration being 14.2 months. The presenting symptom in this group was variable. In many cases, there were absolutely no symptoms which might arouse suspicion of an epithelioma. Eleven of these cases had irregular intermenstrual bleeding. The remaining six patients' complaints included profuse menstrual bleeding, abdominal mass, and dysmenorrhea. The presence of a carcinoma was completely unsuspected in eleven cases.

Additional pathology included two cases with polyps, and nine with fibroids. Both of these conditions are capable of producing abnormal vaginal bleeding.

Case 1 of this Group is of especial interest because of the prolonged course and superficial involvement. The occurrence of malignant change in cervical polyps is unusual. The rarity of this lesion is attested to by the sporadic case reports of such transformations. The nature of the original lesion in this case was overlooked. A two-year latent period ensued without symptoms. A correct diagnosis was finally arrived at, only after repeated biopsies had been taken. Throughout the course the lesion remained superficial and spread laterally. In reviewing the material on this case, it was suspected that the lesion might be Bowen's disease. However, on careful study and serial sectioning, the resemblance to Bowen's disease was found to be superficial. The response of a lesion of this type to inadequate doses of radium is well illustrated by the clinical course.

Case 2 resembles the first case in many respects. The lesion apparently began in a polyp and spread laterally. This patient received 7,000 mg.-hours of radium and has been free of symptoms and recurrence now for six years.

Cases 4 and 5 received no therapy other than biopsy. The lesions were small but definite. Probably the entire lesion was removed in both instances. Both of these patients were followed for five years but have been lost subsequently.

Case 6 is of interest inasmuch as the patient probably had this early epithelioma at the time of her spontaneous abortion. Danforth³ has reviewed the subject of pregnancy complicated by cervical carcinoma and points out that not infrequently spontaneous abortion occurs.

Cases 7 through 13 inclusive had a supravaginal hysterectomy and Cases 15 and 17 had a complete hysterectomy. Only three of these patients complained of intermenstrual bleeding. All had fibroids. In the three cases where the cervixes were notably diseased, two complete hysterectomies, a cervical amputation, and supravaginal hysterectomy were done. Clinically, carcinoma was unsuspected in these cases. Fortunately, in each instance, a preliminary curettage of the cervix as well as of the endometrial cavity were performed. Again, grossly there was nothing suspicious about the curettings. Had a supravaginal hysterectomy been performed without a curettage, these patients would have returned subsequently and been classified as carcinomas of the cervical stump.

All these patients received radium in doses varying from 2,400 mg.-hours to 7,000 mg.-hours. This was followed by deep x-ray therapy. Case 8 lived only three years, dying of massive extension throughout the pelvis. Case 13 lived for nine years. She had had considerable deep x-ray therapy and a persistent vesicovaginal fistula, probably from a radium burn. Clinically, there was never evidence of recurrence. She was taken to Harlem Hospital where a diagnosis of intestinal obstruction was made. Operation was refused.

Although many of the cases are rather recent, it appears from the follow-up of the earlier cases that these superficial epitheliomas develop slowly and are relatively benign, as compared with the more obvious larger lesions involving the portio vaginalis. The site of all of these lesions was just at or within the internal os. In Cases 15 and 17, the lesions were well up in the cervical canal. The presence of squamous epithelium in cervical tissue is not uncommon in chronic cervicitis and polyps of long standing.

This question of squamous metaplasia or epidermidization of the cervical mucosa is of considerable interest. Robert Meyer's original work on congenital erosions of the cervix and the embryology of the cervix and vagina,⁵⁻⁶ has thrown considerable light on the subject and has aided pathologists in explaining the presence of squamous epithelium in cervical glands. Meyer has demonstrated small nests of squamous epithelial cells from the basal zone lying just beneath the cylindrical cervical epithelium in both adults and young children. He has demonstrated the fact that during the third and fourth months of

fetal life, the cervix presents squamous epithelium throughout at least two-thirds of its length. It is not until the sixth month of fetal life that the columnar epithelium replaces the squamous cells. A reversal of this interplay of epithelial cells occurs again in infancy and childhood, and it is not until puberty that the cervix is finally covered throughout by columnar epithelium. During these cyclic alterations, small nests of squamous cells from the basal layer might well become trapped and lie dormant for variable periods of time until trauma, infection, or some other stimulus resulted in active growth. Meyer believes that all types and degrees of squamous metaplasia can be explained on this basis. Many authors have considered squamous metaplasia as a stage in the process of healing of cervical erosions.^{1, 2, 5-7} However, only a small percentage of cervical erosions reveal metaplasia. Another possibility in the etiology of squamous metaplasia, is the upward extension of strands of squamous epithelium from the portio following trauma. Evidence for this mode of development has not been well substantiated. A third possibility is the direct transformation of columnar epithelium to squamous epithelium. This process has been noted in advanced chronic inflammatory processes elsewhere in the body. The evidence to date seems to favor the first and third of the theories. Ribbert,⁹ in discussing epidermidization of the cervix, favored this process as the origin of the majority of squamous epitheliomas of the cervix. Within recent years, this process has been considered benign. In the majority of cervixes showing squamous metaplasia, there is little to suggest carcinoma, when one notes the orderly cellular arrangement and uniformity of the cells. Undoubtedly the increased interest in the early diagnosis of cervical carcinoma has led to more thorough care in handling chronically infected and lacerated cervixes presenting this metaplastic change. This, in turn, has resulted in the eradication of a pathologic process which has the potentialities of carcinogenesis.

Among 459 polyps from the Sloane gynecological service, fifty-three showed evidence of metaplasia. Of these, only two were malignant. Since 1927, the diagnosis of squamous metaplasia of cervical tissue has been made 232 times. In none of these lesions, except those cases herein reported, was there any evidence of carcinoma. Thirteen of our cases of early, superficial epitheliomata are in areas of squamous metaplasia. The evidence substantiates Wollner's⁸ belief that this process is not as benign a lesion as it has seemed to many investigators in recent years.

In none of the cases reported in this paper was there found any deep invasion. It is impossible to predict how long a latent period of intra-epithelial development and superficial surface spread will last, and when rapid growth and invasion will become manifest. Only one of our cases (Case 8) died of extension of the disease. The original tissue

showed malignant metaplasia in practically all of the cervical glands. Her symptoms had been present for one year.

It should be emphasized that the quantity of material removed from the cervical canal by curettage in chronically infected cervixes, which present epidermidization, is rather more abundant than one would expect. Curettings from normal or only mildly infected cervixes generally are scanty or absent, consisting of shreds of normal squamous epithelium or scraps of fragmented cervical epithelium and glands. It is possible that, with a thorough curettage, the entire hyperplastic and metaplastic cervical epithelium may be removed. Perhaps such therapy results in the removal of tissue which, if left in situ for a sufficiently long time, might develop into the typical epithelioma by stages of progressive metaplasia. We have recently observed one patient who had a curettage, supravaginal hysterectomy and bilateral salpingo-oophorectomy. The curettings consisted entirely of hyperplastic and metaplastic cervical glands which showed no epitheliomatous alterations. Six weeks after her operation, the cervical canal measured 2.5 cm. in length, and a curettage produced no tissue whatsoever. Had she not had a thorough curettage at her first operation, it is conceivable that in the future she might return with a cervical stump epithelioma. The appearance of the curettings in Cases 15 and 17, suggest that more than one area of metaplasia may develop into epitheliomata forming small, isolated, discrete lesions or multicentric foci of superficial cancer. When these lesions begin to develop rapidly, after a latent period of 18 to 24 months or longer, they may account for some of the more virulent, rapidly progressing epitheliomata of the cervix which do not seem to respond to radium. (See Case 8.)

Schiller,⁴ in his paper describing the iodine test, points out the latent period in the rate of growth of cervical epitheliomata. The early stage may last for long periods of time and then rapid development ensue. Squamous metaplasia may be the earliest phase of this process. Both Schiller and Schmitz, in discussing the former's paper,⁴ emphasize the distinct cytologic alterations that occur in an epithelioma before invasiveness develops. The latent period before invasiveness becomes manifest undoubtedly varies from patient to patient, depending possibly on local tissue resistance and other unknown factors.

As far as prevention and therapy are concerned, there is no doubt that when removal of a uterus is indicated, the complete hysterectomy, either by the vaginal route or from above, is the operation of choice, especially in the presence of a diseased cervix. Probably many of the stump epitheliomata reported were present at the time of supravaginal hysterectomy. When the diagnosis is made from biopsies, polyps, curettings or trachelorrhaphy tissue, the conventional use of radium and deep x-ray would seem to be the method of choice. Among 538 cervical epitheliomata on file in this Hospital, 38 or 7.1 per cent were stump carcinomata. Of these, three of the patients had supravaginal

hysterectomies here. Thirty-four per cent of these cases appeared within two years following hysterectomy. The cases which were discovered immediately are reported here.

Superficial noninvasive epitheliomata of the type characterized by this group of cases, present occasionally a superficial resemblance to Bowen's disease. On several occasions the term Bowenoid epithelioma has been used. However, on careful study of the microscopic sections many differences are found. The hyper- and parakeratosis is lacking. Although the Malpighian zone is hypertrophied, acanthosis is not usually present. Both lesions present a disorderly cellular pattern, but this group of cases does not show the characteristic nuclear clumping and numerous corps rondes found in Bowen's disease. These lesions, over a period of time, show invasiveness, as evidenced by violation of the basement membrane. In Bowen's disease this has not been described, even though the disease has been present for many months or years, unless a definite transformation into a typical squamous cell epithelioma has occurred.

It is evident that the cervix cannot be regarded as free of disease no matter how clean and apparently healthy it appears. Many of these lesions occurred within the cervical canal, completely out of sight in regions not accessible to the iodine test or the colposcope.

This study has emphasized again the importance of careful microscopic examination of all tissues removed at curettage or biopsy. The importance of curetting separately the cervix and uterine cavity, and the segregation of these curettings for embedding and cutting, as has been often mentioned by Hyman and Corsecaden, should be noted. No less important is the correct orientation of the tissue before fixation, and the frequent need for recutting blocks in order to visualize tissues at deeper levels.

Summary

Seventeen cases of superficial epitheliomata of the cervix have been reported.

Conclusions

1. Early superficial noninvasive epitheliomata of the cervix occur more frequently than supposed.
2. These lesions not infrequently have arisen in tissue which has undergone squamous metaplasia.
3. These lesions tend to develop slowly over a relatively long period of time and seem less malignant than the more obvious epitheliomata.
4. These lesions should be treated as vigorously as the more obvious epitheliomata whether by radiation or surgery, or a combination of the two.

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FIBROIDS IN PREGNANCY

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IT IS an old clinical observation that uterine fibroids enlarge during pregnancy. In both American^{1-9, 18} and British literature^{10, 11, 15, 19} this enlargement has been attributed chiefly to actual hypertrophy of the muscle fibers of the fibroid. The fact that the uterine musculature hypertrophies physiologically during pregnancy has led to the assumption that the smooth muscle fibers of fibroids share in this process. The experimental production of fibroids in rodents by the use of estrogenic substances¹⁶ has contributed to this viewpoint. To quote a recent American textbook:² "The same hormonal stimulus which produces hypertrophy of muscle fibers in the uterine wall stimulates the growth of muscle cells of the tumor." In addition, some authorities have described an increased blood supply during pregnancy as contributing to a general "plethora" of the pelvic organs in which the fibroids participate and consequently enlarge. It is known, however, that degenerative changes on the basis of poor vascular supply are more apt to occur within fibroids during pregnancy.¹⁷ The two conditions are not entirely compatible.

Novak¹⁴ has thrown some doubt upon the clinical observation that fibroids increase in size during pregnancy. Emge²⁰ in a survey of his own material concluded that only a few fibroids reach a considerable size in pregnancy, although he described hypertrophy of muscle fibers within fibroids. Other investigators²⁰ (Bell, Scipiadès, Koster, Katz, Walther, Benner, and Young) believe that pregnancy does not stimulate the growth of fibroids. Adair² and Emge²⁰ state that there is no hyperplasia of connective tissue cells within fibroids during pregnancy so that any enlargement cannot be explained upon this basis.

Material

Since 1926, in this clinic, there have been seventeen cases of uterine fibroids removed in the presence of pregnancy (Table I). Eleven of the patients were multigravidas and six were primigravidas. In eight

of these patients pregnancy was terminated by cesarean hysterectomy (Porro) (viable fetuses), one by myomectomy and hysterotomy, and eight by hysterectomy (nonviable fetuses). The fibroids measured between 1.0 and 15.0 centimeters in diameter and numbered as high as 30 in a single uterus.

TABLE I. ESSENTIAL DATA IN CASES OF FIBROIDS OCCURRING DURING PREGNANCY

AGE	PARITY	GESTATION LUNAR MONTHS	FEVER	SYMPTOMS	PORRO	HYSTERECTOMY ABDOMINAL	MYOMECTOMY	NUMBER OF FIBROIDS	MAXIMUM DIAMETER	DEGENERATIVE CHANGES
35	*M	10	0	0	+			Few	Small	0
35	M	3	+	+		+		3	1.5 cm.	+
38	M	2	0	0		+		4	1.0 cm.	0
30	M	10	0	0		+		1	Small	0
24	M	10	0	0	+			2	1.0 cm.	+
40	†P	9	0	0	+			30	3.0 cm.	+
35	M	10	0	0	+			5	11.0 cm.	+
29	P	4	0	+		+		2	8.0 cm.	+
36	P	5	0	+			+	5	15.0 cm.	+
35	P	10	0	0	+			Many	2 to 3 cm.	+
34	M	2½	+	+		+		3	15.0 cm.	+
32	P	10	0	0	+			Few	Small	+
39	P	5	0	0		+		6	10.0 cm.	0
43	M	2½	0	0		+		Many	3.0 cm.	0
38	M	5	0	0		+		Many	Small	0
32	M	7	0	0	+			Many	2.0 cm.	+
34	M	7	0	0	+			1	Small	0

*Multigravidas.

†Primigravidas.

Case 1.—32-952—B. A., aged 24 years, para 1, gravida 2, was admitted in May, 1932, with a history of a previous cesarean section. Her last menstrual period was August 3, 1931, and the expected date of confinement was May 10, 1932. Pelvic measurements were normal. The blood pressure was 140/90 and there was a trace of albumin in the urine. At the time of operation, fibroids were discovered so hysterectomy was performed following cesarean section. The postoperative course was afebrile. Grossly, the specimen showed only two small subserous fibroids one centimeter in diameter in the region of the right cornu.

Microscopic.—There is considerable red degeneration in the central portions of the fibroid nodules. The uterine muscle fibers beyond the capsule are markedly hypertrophied. The interlacing muscle and connective tissue fibers which make up the fibroid nodules show no hypertrophy or unusual mitotic activity. (See Figs. 1 and 2.)

Case 2.—38-1354—R. H., aged 40 years, para 0, gravida 1, was admitted on May 21, 1938, with premature rupture of the membranes but no pains. Her last menstrual period was on September 20, 1937, and the expected date of confinement was June 27, 1938. Examination disclosed normal blood pressure, normal urine, and funnel type pelvis. At the time of cesarean section, hysterectomy was performed because a number of small subserous nodules were found. Examination of the gross

specimen disclosed numerous subserous and intramural fibroid nodules. There were approximately thirty such tumors varying between 2.0 and 3.0 centimeters in diameter.

Microscopic.—The fibroid nodules are made up of interlacing muscle and connective tissue fibers which show no hypertrophy or unusual mitotic activity. There is moderate hyaline degeneration. The uterine muscle cells are markedly hypertrophied. (See Figs. 3 and 4.)

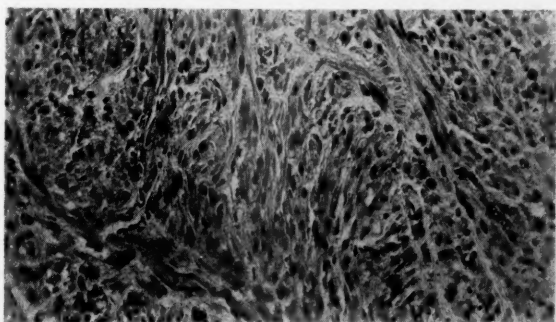


Fig. 1.—Case 1—Photomicrograph, $\times 200$, of fibroid. There is no hypertrophy of the smooth muscle fibers. Compare this with Fig. 2.

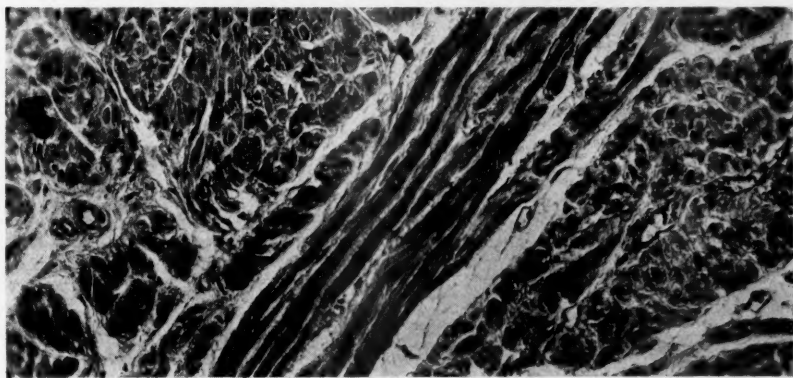


Fig. 2.—Case 1—Photomicrograph $\times 200$ through a section of uterine muscle. Note enormous hypertrophy of muscle cells as compared with those in Fig. 1.

Case 3.—38-1038—B. H., aged 35 years, para 5, gravida 6, was admitted on April 16, 1938. Her last menstrual period commenced on July 20, 1937, and the expected date of confinement was April 27, 1938. On admission, blood pressure of 140/90, normal urine, normal pelvic measurements and near term pregnancy were found. Pelvic examination disclosed a hard, irregular, tumor mass behind the cervix. The patient went spontaneously into labor and two hours later was delivered by cesarean hysterectomy. Examination of the gross specimen disclosed a nodular, well-encapsulated mass eleven centimeters in diameter attached to the posterior surface of the uterus. Four other nodules about four centimeters in diameter were found in the uterine wall.

Microscopic.—The fibroid is made up of interlacing bands of smooth muscle and fibrous connective tissue which show no hypertrophy or unusual mitotic activity. Hyalin degeneration is present.

Case 4.—41-2869—I. R., aged 29 years, para 0, gravida 2, was admitted in September, 1941, with amenorrhea of two months' duration and lower abdominal pain. Her last menstrual period commenced July 5, 1941, and the calculated date of expectancy was April 12, 1942. At the time of admission, the temperature was normal, white blood count was 10,000, and pelvic examination disclosed two separate masses, the anterior of which was quite soft. A Friedman pregnancy test was positive. Total abdominal hysterectomy was performed and the postoperative course was afebrile. Examination of the gross specimen showed two fibroid nodules, the largest being eight centimeters in diameter.



Fig. 3.—Case 2—Photomicrograph $\times 200$ of fibroid. There is considerable fibrous tissue but no hypertrophy of smooth muscle fibers. Compare this with Fig. 4.



Fig. 4.—Case 2—Photomicrograph $\times 200$ through a section of uterine musculature. As in Fig. 2 note hypertrophy of smooth muscle fibers. Compare with Fig. 3.

Microscopic.—There is red degeneration in the center of the fibroid. The fibroid is composed of interlacing bands of smooth muscle and connective tissue fibers which show no hypertrophy or increase in mitotic activity.

Case 5.—37-362—L. S., aged 36 years, para 0, gravida 1, was admitted in February, 1937, complaining of upper right quadrant pain. Her last menstrual period commenced on September 12, 1936, and the expected date of confinement was June 19, 1937. Examination disclosed a 5 months' pregnant uterus with a large fibrôid, normal temperature, and a white blood count of 15,200. Abdominal hysterotomy and multiple myomectomy were performed. The postoperative course was complicated by considerable abdominal distention and a febrile course. The gross specimen consisted of numerous uterine fibroids which had been removed from the uterus. The largest measured fifteen centimeters in diameter and the cut section showed numerous, degenerated areas of gelatinous and serous material.

Microscopic.—There are marked red degenerative changes present. There is some edema separating the bundles of smooth muscle and fibrous tissue but there is no hypertrophy or unusual mitotic activity.

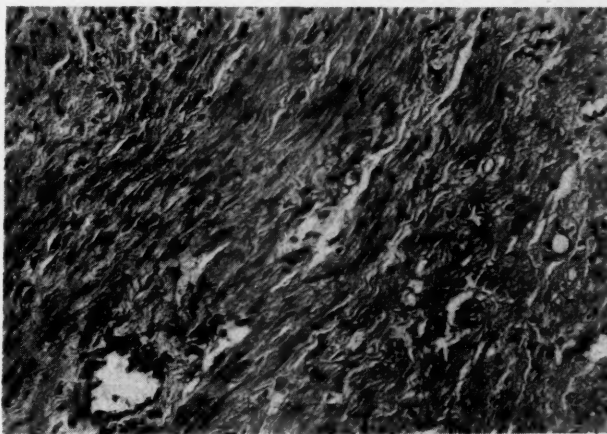


Fig. 5.—Photomicrograph $\times 200$ of fibroid removed from a nonpregnant woman. Compare with Figs. 1 and 3, of fibroids removed from pregnant woman. Note similarity.

Case 6.—36-1787—I. F., aged 35 years, para 0, gravida 1, was admitted in July, 1936, at term with controlled diabetes. Her last menstrual period commenced on September 25, 1935, and the expected date of confinement was July 2, 1936. Cesarean hysterectomy was performed. Gross specimen consisted of a uterus which measured 12 by 16 by 8 centimeters. There were several small, hard, white nodules beneath the serosa.

Microscopic.—The fibroid nodules show red degeneration. The smooth muscle and connective tissue fibers which make up the fibroids show no hypertrophy or unusual mitotic activity.

Case 7.—31-1096—I. K., aged 30 years, para 1, gravida 2, was admitted in May, 1931. Her last menstrual period commenced in October, 1930, and the expected date of confinement was believed to be sometime in June, 1931. The patient went into labor and was delivered spontaneously of a 3,350 gram, male infant. During the puerperium subtotal hysterectomy was performed for fibroids and sterilization.

Microscopic.—Involuting, hypertrophied, uterine muscle fibers are present. The fibers which make up the fibroid show no hypertrophy.

Case 8.—36-2947—D. S., aged 38 years, para 1, gravida 2, was admitted in November, 1936, with hypertension, albuminuria, and decreased kidney function. The last menstrual period commenced on September 23, 1936, and the expected date of confinement was June 30, 1937. Interruption of pregnancy was decided upon and subtotal hysterectomy was performed. Gross examination revealed four small tumor masses about one centimeter in diameter in the myometrium.

Microscopic.—Uterine muscle fibers show slight hypertrophy. The fibroid is composed of interlacing smooth muscle and connective tissue fibers which show no hypertrophy or unusual mitotic activity. No degenerative changes are present.

Case 9.—36-535—R. B., aged 35 years, para 2, gravida 6, was admitted in March, 1936, with lower right quadrant pain, temperature of 100 degrees and white count of 11,800. Her last menstrual period commenced on December 30, 1935, and the expected date of confinement was October 6, 1936. Pelvic examination disclosed the uterus to be irregularly enlarged to the size of a three months' gestation. A Friedman test, however, was negative upon two occasions. Total hysterectomy was performed. Gross examination disclosed a three months' intrauterine pregnancy and three hard, white nodules measuring up to 1.5 centimeters in diameter.

Microscopic.—There is moderate hypertrophy of the uterine fibers. There is some red degeneration within the fibroid nodules but no hypertrophy of the muscle fibers or increased mitotic activity.

Case 10.—34-1716—D. C., aged 35 years, para 2, gravida 3, was admitted in July, 1934, with slight hypertension, edema and marked diastasis recti. Her last menstrual period commenced on September 30, 1933, and the expected date of confinement was July 6, 1934. Cesarean hysterectomy (Porro) was performed. Gross examination showed a few, small, pinkish-white nodules over the anterior surface of the uterus.

Microscopic.—The uterine muscle fibers are markedly hypertrophied. The fibroid is made up of muscle and connective tissue fibers which show no hypertrophy or unusual mitotic activity.

Case 11.—26-670—G. W., aged 34 years, para 4, gravida 5, was admitted in July, 1926, with abdominal pain and a history of vaginal bleeding. Her last menstrual period commenced on May 1, 1926, and the expected date of confinement was February 8, 1927. Pelvic examination disclosed a tender, cystic mass posterior to the uterus. Hysterectomy was performed. Grossly, the specimen consisted of a two and one-half months' gravid uterus with three attached fibroids, the largest being 15 centimeters in diameter. Cut section showed gross degenerative changes in the large fibroid.

Microscopic.—The uterine muscle fibers show beginning hypertrophy. The muscle and connective tissue cells which make up the fibroid nodules show no increase in size. There is marked red degenerative changes in the large fibroid.

Case 12.—37-80—Z. S., aged 32, para 0, gravida 1, was admitted on September 18, 1936, with a history of myomectomy performed in April, 1936. Her last menstrual period commenced on December 24, 1935, and the expected date of confinement was October 1, 1936. Because of the

recent myomectomy, cesarean hysterectomy was performed. No microscopic report is available although several small fibroids which showed gross degeneration were present.

Case 13.—38-679—I. C., aged 39 years, para 0, gravida 2, was admitted in March, 1938, with a history of pyelitis, hypertension and albuminuria. Her last menstrual period commenced on October 18, 1937, and the expected date of confinement was July 25, 1938. Subtotal hysterectomy was performed. Gross examination revealed a tumor mass 10.0 centimeters in diameter on the posterior surface of the uterus with several other well circumscribed fibroids in the wall.

Microscopic.—There is moderate hypertrophy of the uterine muscle fibers but no hypertrophy or unusual mitotic activity of the fibers within the fibroid.

Case 14.—40-2752—D. G., aged 43 years, para 8, gravida 10, was admitted in September, 1940, because of a pelvic tumor. The last menstrual period commenced on August 10, 1940, and the expected date of confinement was May 17, 1941. Pelvic examination revealed a nodular, enlarged uterus. Hysterectomy was performed. Gross examination revealed a pregnant uterus, greatly distorted by fibroids, the largest being about 3.0 centimeters in diameter.

Microscopic.—The uterine muscle fibers show mild hypertrophy. There is no hypertrophy or unusual mitotic activity of the fibers within the fibroid.

Case 15.—40-2652—D. C., aged 38 years, para 1, gravida 2, was admitted in September, 1940, complaining of lower abdominal pain. Her last menstrual period commenced in April, 1940, and the expected date of confinement was believed to be in January, 1941. Hysterectomy was performed. Grossly, the uterus had several small myomata within its wall.

Microscopic.—Moderate hypertrophy of the uterine muscle fibers was present. There is no hypertrophy or unusual mitotic activity of the fibers which make up the fibroid.

Case 16.—42-806—I. A., aged 32 years, para 3, gravida 4, was admitted in January, 1942, with severe hypertension and albuminuria. Her last menstrual period commenced on July 18, 1941, and the expected date of confinement was April 25, 1942. Hysterectomy was performed. Gross examination revealed numerous fibroid nodules measuring 1.0 to 2.0 centimeters in diameter. Some of these showed hemorrhagic areas upon cut section.

Microscopic.—Marked hypertrophy of the uterine muscle fibers is present. No hypertrophy of the muscle fibers or unusual mitotic activity among the connective tissue fibers of the fibroid was noted. Some red degeneration is present.

Case 17.—38-1843—G. D., aged 34 years, para 1, gravida 2, was admitted in June, 1938, with hypertension and albuminuria. Her last menstrual period commenced on November 17, 1937, and the expected date of confinement was August 24, 1938. After failure at bag induction a Porro section was performed. Gross examination disclosed a single, small subserous fibroid attached to an infected puerperal uterus.

Microscopic.—The uterine muscle fibers showed marked hypertrophy. There is no hypertrophy of the fibers which make up the fibroid nodule.

(In reporting the histories of the above cases, we have made no attempt to justify the indications for the operative procedures employed.)

Comment

Degenerative changes of some degree were present microscopically in ten of the seventeen cases. There was no evidence of hypertrophy of the muscle fibers within the fibroids (Figs. 1, 2, 3, 4), and no hyperplasia of the connective tissue cells as evidenced by unusual mitotic activity. Significant edema could be seen in only one of the fibroids. None of the fibroids showed any increase in the size and number of blood vessels when compared to fibroids removed from nonpregnant patients (Fig. 5). All slides had been stained with routine hematoxin and eosin.

The alleged enlargement of fibroids during pregnancy has been explained on one or a combination of the following factors:

(1) There is hypertrophy of the muscle cells within the fibroids. We do not believe that such hypertrophy occurs and have been unable to demonstrate its presence in any of the seventeen cases studied. (See Figs. 1, 2, 3, 4.)

(2) There is hyperplasia of the connective tissue stroma within the fibroids. In our series no unusual mitotic activity was present, and other investigators^{2, 20} have disclaimed any such hyperplasia as contributing to fibroid enlargement during pregnancy.

(3) It has been suggested that with the growth of the uterus out of the pelvis, the fibroid becomes more easily palpated abdominally and, therefore, more prominent. Due to pressure of the enlarging uterine contents, many fibroid nodules in the uterine musculature become flattened and give the clinical impression that they have increased in size. It is our opinion that any enlargement of asymptomatic fibroids during pregnancy is apparent rather than real.

(4) The fibroids enlarge because of edema and vascular engorgement. One of our seventeen specimens showed significant edema microscopically. It has been suggested that edema as a result of severe degenerative changes may account for enlargement. These degenerative changes would necessarily be accompanied by symptoms. Bonney,¹² who has had probably the greatest experience with myomectomy during pregnancy, observes: "As a rule the hypertrophy of fibroids during pregnancy is not very marked. When the seat of certain degenerative changes, the increase may be obvious, and is a sign that the tumor has become edematous." Asymptomatic fibroids probably do not enlarge during pregnancy beyond their normal rate of growth, since edema (from severe degenerative changes) is not present in the absence of symptoms. Campbell¹⁷ states that 78 per cent of fibroids during pregnancy show degenerative changes of some degree and only 7.8 per cent show it at other times. Mussey¹⁸ reported a series of thirty-two fibroids removed during pregnancy, with twenty-one showing some degeneration. This evidence of poor vascular supply is hardly consistent with increased growth of fibroids during pregnancy.

Conclusions

1. There is no hypertrophy of the smooth muscle fibers or hyperplasia of the connective tissue stroma within fibroids during pregnancy.
2. Approximately fifty to seventy-five per cent of all fibroids during pregnancy show degenerative changes. Probably most fibroids during pregnancy have a poor blood supply and show little actual growth.
3. Edema on the basis of severe degenerative changes could explain the enlargement of fibroids during pregnancy. However, this enlargement should be accompanied by symptoms.
4. Any suspected enlargement of asymptomatic fibroids during pregnancy is only apparent.

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THE EFFECT OF PREGNANCY AND PUERPERIUM ON THE THIAMINE STATUS OF WOMEN*

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THERE is considerable evidence in support of the concept that all substances needed in the growth and development of the fetus are supplied from the maternal tissues even when the dietary is inadequate. However, malnourishment during the pregnancy period may arrest the growth and development of the fetus, and even cause prenatal or postnatal death. Because of the intimacy of development it is not yet possible to determine directly the nutritional needs of the fetus during the prenatal period, and one must assume that in meeting the maternal needs the requirements of the fetus will also be met.

Researches with animals indicate that the optimum growth and development of the fetus necessitate a maternal dietary abundantly rich in vitamins, minerals and protein. The exact requirements of women in pregnancy are not known, but reports have been made to the effect that the need for iron increases two to tenfold¹ and that the need for thiamine may be five times that of nonpregnancy⁶ (also Table I).

The present research was conducted in an effort to obtain an exact measurement of the effect of pregnancy and early puerperium on the thiamine status of women.

TABLE I. ESTIMATES OF THE THIAMINE REQUIREMENTS DURING PREGNANCY AND LACTATION

	REQUIREMENTS (MG.) FOR PREGNANCY	LACTATION
League of Nations ²	0.5 to 0.8	0.5 to 0.8
Baker and Wright ³	3 to 5 times normal	
Dieckmann and Swanson ⁴	1.8	--
Cowgill ⁵	--	1.4 to 2.1
Toverud ⁶	4 to 5 times normal	
Rose ⁷	--	1.5 to 1.8
National Research Council ⁸	1.8 (late)	2.3
Williams et al. ⁹	1.4	--

Literature

Using a synthetic diet containing just enough vitamin B complex to ensure growth and conception, Moore and Brodie¹⁰ found that female rats frequently aborted or resorbed their fetuses, and that the young which were born usually died before weaning, exhibiting a disorder resembling polyneuritis. Evans and Burr¹¹ have shown that the lactating rat may require five times as much thiamine to nurse her

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litter successfully as to maintain the maternal organism. Because the high mortality of nursing rats was considerably reduced by feeding the vitamin B complex to the young, Sure¹² concluded that the transfer of these vitamins into the milk is rather inefficient. In earlier studies he had shown that thiamine is the most important of the B-vitamins studied for the promotion of successful lactation, due to its capacity to stimulate appetite and copious milk flow. Shin¹³⁻¹⁵ studied the transfer of thiamine from the maternal tissues to the fetus and to the mammary glands of rabbits, rats and mice. A dietary partially deficient in thiamine caused the estrus cycle to become erratic or disappear. If conception occurred, abortion was likely. If the young were born alive, they showed symptoms of thiamine deficiency. It is not appropriate to review here all the literature based on animal experiments with thiamine during pregnancy. The evidence clearly indicates that pregnancy increases the thiamine needs and that rats may require perhaps five times as much thiamine for successful pregnancy and lactation as for growth.^{10-11, 16-18}

Strauss and McDonald¹⁹ reported that pregnancy unmasks latent beriberi in women and that the polyneuritis of pregnancy is probably a dietary disorder. Subjects with pregnancy eclampsia generally exhibit thiamine deficiency²⁰ which is accompanied by subnormal levels of thiamine in the placental tissues. Beginning with the fourth month of pregnancy Hildebrandt and Otto²¹ injected large doses of thiamine intravenously and were not able to measure significant amounts of thiamine in the urine of women until after the child had been born, indicative of rather severe thiamine inadequacy. A similar result is reported by Neuweiler²² who reported the retention of large proportions of parenteral doses of thiamine, especially when the subjects manifested "toxemia," again indicating thiamine insufficiency. Also, it has been shown²³ that 12 per cent of the pregnant women studied showed electrocardiogram evidences of thiamine deficiency. These citations from the clinical literature serve to show that evidence is slowly accumulating which indicates that the thiamine requirements of women in pregnancy are rather high.

Toverud⁶ observed that 46 per cent of the 114 pregnant women studied normally excreted no thiamine in a 24-hour urine sample. In eight of ten subjects given a test dose of 5 mg. no thiamine was detected in the urine by thiochrome assay. When four women were given 1 to 3 mg. daily for 5 to 17 days, no significant excretion was noted and it was necessary to give 4 to 5 mg. daily to produce as high an excretion as was measured in a nonpregnant control group. It was concluded that pregnancy had increased the thiamine requirements four- to fivefold. Similar tests on women who had been lactating two to four months, resulted in a higher excretion of test dosages of 5 mg. which was interpreted to indicate that the lactation requirements for thiamine are only slightly higher than those of nonpregnancy.

Methods for Measuring Thiamine Status

The literature discloses that the thiamine status may be measured by estimating the thiamine, pyrimidine or pyruvic acid content of the blood or urine, either with or without the administration of small or large test dosages of thiamine, given parenterally or by mouth, and that these compounds may be measured by colorimetric, fluorimetric, biologic or microfermentation procedures. When this research was

initiated (1940), a thorough study was made of these various possibilities and as a result a technique was evolved which, in our hands, produced reliable data. In this research the quantity of thiamine needed to produce the same excretion status on successive lunar months during late pregnancy and early puerperium was measured.

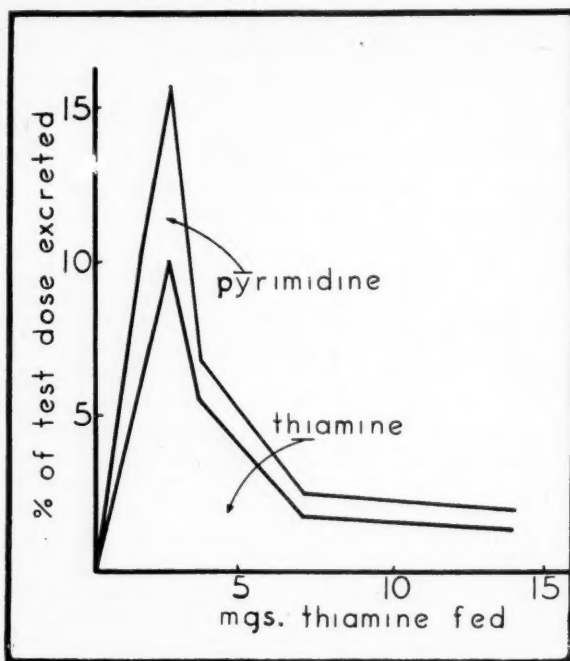


Fig. 1.—Excretion of test doses of thiamine expressed in terms of thiamine and of thiamine plus pyrimidine. Pyrimidine excretion parallels thiamine excretion.

Experimental Procedure

Injection Series.—The subject is given a supper low in thiamine content at 5 P.M. At 8 P.M. she voids her urine, then collects all urine passed up to 7 A.M. on the following morning. Collections are made into two-liter bottles containing 10 c.c. of 10 per cent sulfuric acid, to hold the acidity of the urine below pH 4 and preserve the thiamine content for at least 48 hours. At 7 A.M. the pooled urine sample is taken to the laboratory and refrigerated (5° C. or less), then analyzed by the modified microfermentation procedure²⁴ to determine the thiamine and pyrimidine excretion during a basal eleven-hour period. It has been determined that the basal excretion is approximately the same from day to day when a subject is living on an institution dietary.

Having established the basal excretion, the same procedure is repeated on the following night. This time, however, the subject is given an intramuscular injection of thiamine solution. On successive nights these injections are progressively increased until urine analysis shows that the "excretion peak" has been passed, the excretion peak being the point at which the highest proportion of the administered thiamine is excreted (Fig. 1). At the end of each succeeding lunar month the basal excretion and excretion peak of the subject are again determined. The dosage is increased each month according to the

following schedule which was worked out on a preliminary group of twenty subjects:

LUNAR MONTH OF PREGNANCY	MG. THIAMINE TO BE INJECTED ON SUCCESSIVE DAYS					
	1ST DAY	2ND DAY	3RD DAY	4TH DAY	5TH DAY	6TH DAY
7	0	.25	.50	.75	1.00	1.25
8	0	.25	.50	.75	1.00	1.25
9	0	.50	.75	1.00	1.25	1.75
10	0	.75	1.25	1.75	2.50	5.00
PUERPERIUM	0	.75	1.25	2.50	3.00	5.00

Najjar and Holt²⁵ have shown that the major part of an intravenous injection of 1 mg. of thiamine is excreted within two hours, and that after four hours the excretion is nearly completed. McAlpine and Hills²⁶ found that when 1 mg. of thiamine was fed, the excretion was nearly completed in three hours. Melnick and Field²⁷ have also observed a prompt excretion of test doses.

Ingestion Series.—The technique for ingestion studies is identical with that of the injection series, except that the thiamine is fed, preferably in tablet form. The dosages are increased on successive months and on successive days of each test period as follows:

LUNAR MONTH OF PREGNANCY	MG. THIAMINE TO BE FED ON SUCCESSIVE DAYS					
	1ST DAY	2ND DAY	3RD DAY	4TH DAY	5TH DAY	6TH DAY
7	0	0.5	1.0	1.5	2.0	2.5
8	0	0.5	1.0	1.5	2.0	2.5
9	0	1.0	1.5	2.0	2.5	3.5
10	0	1.5	2.5	3.5	5.0	7.0
PUERPERIUM	0	1.5	2.5	5.0	7.0	10.0

Details on This Study

In the present study the thiamine* used in the injection series was dissolved in physiological saline in concentrations of 1 or 10 mg. per c.c. The thiamine used in the feeding tests was fed in 1 grain tablets containing 1 or 5 mg. each. The potencies of these preparations were confirmed by the thiochrome method.²⁸

All of the fifty subjects used in this study were patients at the Florence Crittenton Home in Boston which receives primiparous unmarried women during the seventh lunar month of pregnancy or later. These subjects ranged in age from 14 to 22 years, but the majority were 18 years old. Women with disorders which might interfere with the absorption or metabolism of thiamine were excluded. Unfortunately, it was not possible to study these patients beyond the first puerperal month for they were discharged from the home and could not be further subjected to the strict control necessary for this type of study. Because it was not possible to study these subjects previous to admission, it was necessary that others be used as controls. Since the data show that the early pregnancy requirement is similar to that of nonpregnancy, our inability to study each subject during the entire gestation period is of no consequence.

The thiamine content of the food upon which the subjects subsisted during the investigation was determined each day by fluorimetric assay.²⁸ Food samples were collected by instructing the subject to

*We wish to acknowledge the generosity of Hoffmann-La Roche, Inc., in supplying the thiamine used in this study.

TABLE II. QUANTITIES OF THIAMINE BY MOUTH AND BY INTRAMUSCULAR INJECTION, REQUIRED TO PRODUCE THE EXCRETION PEAK IN SUBJECTS DURING ADVANCING PREGNANCY, AND IN NONPREGNANT CONTROLS. LACTATION PERFORMANCE WAS GRADED "GOOD" WHEN INFANT WAS ENTIRELY BREAST-FED UNTIL DISCHARGE, "FAIR" IF PARTIALLY BREAST-FED UNTIL DISCHARGE, AND "POOR" WHEN TAKEN OFF BREAST EARLY IN PUERPERIUM

SUB- JECT	NONPREG- NANCY	SUB- JECT	LUNAR MONTH OF PREGNANCY				LACTATION PERFORM- ANCE
			8	9	10	PUER.	
I. Feeding Series							
F. P.	0.25 mg.	R. L.		2.5 mg.	2.5 mg.	5.0 mg.	Good
M. N.	.50	M. B.		2.5	3.5	2.5	Poor
P. G.	.50	B. C.		1.5		3.5	Poor
E. W.	.50	P. E.			3.5	5.0	Poor
		P. M.			1.5	1.5	Poor
		M. L.		1.5	2.5	2.5	Good
		G. F.	2.5 mg.	2.5	5.0	4.0	Fair
		E. M.	1.5	1.5	2.5	2.5	Poor
II. Injection Series							
M. N.	0.10	L. K.	1.00	1.00	1.00	2.50	Good
V. T.	.10	L. S.	.75	1.00	1.00	1.75	Good
E. W.	.20	D. G.		.25	.50	.75	Fair
H. S.	.20	P. L.	.25	.50	.75	1.75	Poor
		N. H.		.75	1.25	1.75	Good
		M. H.		1.25		1.75	Good
		M. C.		.50	.75	.75	Fair
		M. W.			.50	.75	Poor

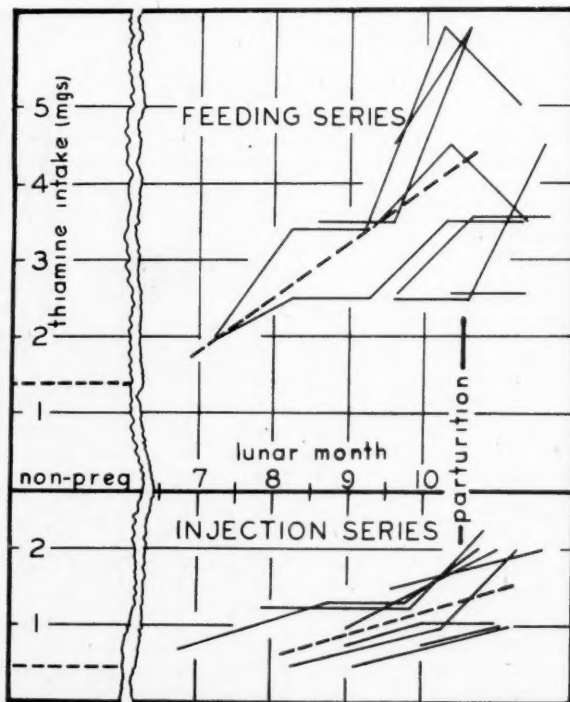


Fig. 2.—Data from Table II plotted with respect to parturition date and thiamine in food. Feeding series represent sum of food thiamine and thiamine fed as supplement while injection series represent calculated injection equivalent of food thiamine plus thiamine injected intramuscularly.

place on an extra plate, amounts of the food equivalent to that which she served herself at each meal. At the end of the meal this food (including milk and all thiamine-containing liquids) was placed in a collection bottle which was refrigerated until analyzed. The thiamine content of the daily dietaries varied between 0.24 mg. and 1.61 mg., and averaged 1.05 mg. and usually ran within 25 per cent of this average.

Discussion

The amounts of supplementary thiamine required to produce an excretion peak in nonpregnant subjects and at various stages of pregnancy are presented in Table II. Approximately one-third as much thiamine was required by intramuscular injection as by mouth to reach this peak in nonpregnant subjects, indicating that thiamine may be one-half as effective by mouth as by injection.

These data are presented in a more useful form in Fig. 2, by inclusion of the food thiamine. In the fed series, the sum of the food thiamine and the supplement represent the total thiamine which produced the excretion peak, and this sum has been plotted. However, in the injection series, thiamine was taken both orally and intravenously, and it has been shown above that thiamine is not equally effective by these routes. So that the results of this series might be evaluated, the amount of thiamine injected was added to one-third of that ingested by each subject, and the total daily thiamine intake is thus expressed in Fig. 2, as though all thiamine had been injected. It is evident in Table II, and Fig. 2, that the amount of thiamine necessary for the production of the excretion peak increased throughout the pregnancy period. In comparison with the nonpregnant control group, the relative increase was essentially the same in the injection series as in the fed series (Table III). Since the same results were obtained when thiamine was administered by two different routes, the above observation is significant and is a measure of a real increase in physiologic requirements. It is not, for instance, the result of an impairment of intestinal absorption resulting from the pregnancy state. Thus it appears that a woman in the tenth lunar month of pregnancy requires three times as much thiamine as in nonpregnancy to reach her excretion peak.

TABLE III. THIAMINE REQUIRED BY INTRAMUSCULAR AND ORAL ROUTES TO PRODUCE EXCRETION PEAKS IN PREGNANT AND NONPREGNANT WOMEN. RATIO OF THIAMINE REQUIRED TO PRODUCE EXCRETION PEAKS IN PREGNANCY, TO THAT REQUIRED IN NONPREGNANCY

PHYSIOLOGICAL STATUS	ROUTE OF ADMINISTRATION	
	ORALLY	INTRAMUSCULAR INJECTION
nonpregnant	1.0	1.0
7th lunar	1.4	--
8th lunar	1.8	1.8
9th lunar	2.6	2.5
10th lunar	2.9	2.9
1st puerperal	2.9	3.6

A typical excretion peak titration is shown in Fig. 1. The upper values represent the total of thiamine and pyrimidine excreted by the subject, while the lower graph presents the proportion of thiamine. It is evident that the excretion peak is a result of the combined effect of thiamine and pyrimidine.

The requirement for excretion peak seems to be the same, whether or not the subject is lactating. Human milk usually contains no more than 0.02 mg. of thiamine in 100 c.c.²⁹ A woman who had taken 3 mg. of thiamine as a daily supplement throughout the pregnancy period produced a milk containing 0.04 mg./100 c.c.,³⁰ but the 25 ounces which she secreted on the 18th postnatal day contained only 0.3 mg. of thiamine.

Although the loss by secretion in the milk is not very significant in terms of the total thiamine needs of the lactating woman, the requirements for milk synthesis may be considerable.

The excretion peak has been produced in all of the fifty-odd subjects studied, pregnant and nonpregnant, thiamine deficient and thiamine sufficient. Nonpregnant subjects with no clinical manifestations of thiamine deficiency and subsisting on a dietary of unvarying thiamine content require the same quantity as supplement from week to week to reach the excretion peak. Subjects showing thiamine deficiency require a larger supplement to attain the excretion peak. After the manifestation of deficiency has responded to thiamine therapy, small amounts of supplement are needed in this excretion test. Women in midpregnancy require slightly more thiamine than nonpregnant women and as pregnancy advances the amount of thiamine to titrate the peak becomes increasingly large. It is evident: (1) that the excretion peak is a normal physiological phenomenon; (2) that the quantities of thiamine needed for its titration are directly proportional to thiamine needs; (3) that this peak can be determined fairly accurately in a subject; and (4) that titration of the thiamine excretion peak is a useful method for (a) measurement of the effectiveness of thiamine therapy, or (b) measurement of relative increase in thiamine needs during physiological stress (such as pregnancy). At present it does not seem that this titration can be used to measure the actual quantity of thiamine needed by a subject, but rather the requirement relative to the normal.

Summary

The oral or intramuscular administration of thiamine to normal subjects causes the percentage excretion of thiamine and pyrimidine in the urine to increase as the dosage is increased on successive days until a peak is reached. Subsequent increases in dosage result in progressively less efficient excretion of thiamine or pyrimidine.

This excretion peak has been observed in all subjects studied, whether normal, thiamine deficient or pregnant. The quantity of thiamine required to titrate this peak appears to be proportional to the thiamine

status, is high for thiamine deficient persons and for women in advanced pregnancy and puerperium, and is low for those who are not deficient.

Thiamine was administered orally and intramuscularly to measure the excretion peaks of sixteen pregnant women. Since approximately three times as much thiamine was needed in titrating the excretion peaks of these subjects during late pregnancy and early puerperium, it is suggested that the requirements for thiamine during pregnancy and lactation are three times those of nonpregnancy.

Acknowledgment

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HEMORRHAGE AS THE MOST IMPORTANT CAUSE OF MATERNAL DEATH*

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THE number of puerperal deaths in the United States is steadily decreasing. In 1941,¹ the year for which the latest figures are available, the rate was 3.2 per 1,000 live births, or 48 per cent lower than 1933, the first year for which complete statistics were compiled. In 30 states the rate was lower, notably Montana (1.6), Washington (1.8), Utah (1.9), Minnesota (2.0) and Connecticut (2.0). The rate was highest in Florida (6.3) and South Carolina (6.2).

The reasons for this welcome reduction are not altogether clear. The trend has been downward since 1929, with sharper decline in the last five years. There can be no doubt that expansion of our national maternal welfare service has played an important part. A nationwide campaign of popular education has not yet reached every woman, and perhaps it is too much to expect that it ever will, though social and public welfare agencies, the radio and press are participating. Not all the information given the public has had merit but, on the whole, good has come of it. Continued education of the physician is, of course, a most important factor, for only when every one who practices obstetrics, consultant and general practitioner alike, can be made to feel that prevention of a single maternal death is an important contribution, will we approach the desired minimal mortality. The studies carried on by medical groups with the close cooperation of vital statisticians, have borne good fruit in many communities, and, I am sure, have had a profound effect upon our national death rate.

The rates for both white and Negro women have declined, but not uniformly. The rates for Negro women in 1940 and 1941 were nearly two and one-half times those of white women. In fact Yerushalmy² has shown that reduction of the rate in 1940 was accounted for entirely by reduction in the rate for white women. Since nearly one-quarter of the deaths in 1940 and 1941 occurred in Negro women, it is obvious that parallel reduction in the rates would effect substantial improvement in the total mortality. However, the high maternal death rates in southern states are not due to the racial factor alone, for the rates for white women are also higher than similar rates in other states.

Rates show significant decline even in large cities, where the racial factor might reasonably be expected to contribute unduly to maternal mortality. In 27 large cities, in half of which more than 10 per cent of the population was colored, the puerperal mortality rate for 1941 was considerably lower than the national rate.³ In New York City, where the rate from abortion is nearly seven times as high in Negro women as in the white, and the Negro puerperal death rate almost three times that of the white, the puerperal death rate in 1941 was 2.2 per 1,000 live births, a reduction of 50 per cent in ten years.

*Read, by invitation, at a meeting of the Boston Obstetrical Society, March 16, 1943.

Comparing our national figures for two five-year periods, 1931 to 1935, and 1936 to 1940, Yerushalmy² finds that percentage reduction was greatest in the infection group (31 per cent) and lowest in the number of deaths due to hemorrhage and shock (16 per cent), with 24 per cent decrease in deaths due to toxemia. This resistance to reduction in the hemorrhage incidence deserves attention.

TABLE I. PUERPERAL MORTALITY, U. S.
PERCENTAGE REDUCTION 1931-1940

		WHITE	COLORED
Infection	31	34	20
Toxemia	24	27	12
Hemorrhage	16	16	8

Statistically infection is responsible for the greatest number of maternal deaths. In 1940, 41 per cent was assigned to this cause, 25 per cent to toxemia, and 23 per cent to hemorrhage, trauma and shock. This is not a complete or wholly satisfactory statement, for it refers to but 89 per cent of the deaths. The remaining 11 per cent was assigned to other and unspecified conditions largely because of inadequate data, though more than half occurred during or after delivery, the usual time for fatal hemorrhage.²

TABLE II. PUERPERAL MORTALITY, U. S., 1940

	PER CENT	NO. DEATHS
Infection	41	3626
Toxemia	25	2250
Hemorrhage, Trauma, Shock	23	2058
Unspecified	11	942

The principal reason for collecting and tabulating these vital statistics is to give us full knowledge of the problem. They are as valuable as the autopsy, since it is necessary to know what women die of before a satisfactory program of prevention can be undertaken. No problem can be solved until it is clearly stated.

Let us look a little more closely at these vital statistics upon which preventive programs depend. In at least 40 per cent, only one cause of death was reported. The accuracy of all the figures depends upon the character and quality of these vital records, yet this information varied widely throughout the United States. In New York and Massachusetts, for example, over 70 per cent of the certificates contained more than one cause, with 31 per cent showing three or more causes, while, only 43.9 per cent in the East South Central States reported more than one cause, and only 12.8 per cent showed three or more. In many of the southern states there was an almost complete lack of detail on the certificates for Negroes.⁴

It is easy to code and tabulate causes of death when but one cause is reported, yet the result may be nothing more than mere arithmetic and of little value in planning well-rounded preventive programs. And even when two or more causes appear, there is still a problem, though a different one, for each death must be tabulated as if it were due to a single cause, and the additional information, valuable though it may be, is lost. It has been caused to disappear by the magic of rules and definitions which assign death to one statistical cause.

No one knows better than the obstetrician that maternal death is often the outcome of a complex sequence of circumstances, and rarely the result of one cause; that hemorrhage is a common and often a repeated incident along the way; that often infection would not occur at all, or that death would not follow it, if blood loss had not been considerable; that sepsis and hemorrhage are obstetric bed-fellows. Always an important factor, whether reported or not, hemorrhage is almost lost in tabulations. If general or local infection, pyelonephritis, thrombophlebitis or embolism and sudden death complicate the case, infection takes precedence over every other puerperal cause, no matter how serious, with the exception of ectopic pregnancy. Toxemia, too, is preferred over hemorrhage, unless placenta previa or placental separation is reported as well. Further, since 1940, deaths attributed to hemorrhage and trauma have been assigned to abortion, if they occurred before the twenty-eighth week of pregnancy, and not to their specific causes as formerly.⁵

Vital statisticians have become aware of the importance of investigating the frequency of contributory causes of death. In fact the Bureau of the Census in 1941, planned to tabulate one associated cause on all certificates reporting two or more joint causes of death. In 1936, there were 12,182 puerperal deaths, 1,398 of which were assigned to hemorrhage by the rules which provide for selection of one cause only. These were the published statistics. By tabulating only the first two causative factors, Janssen⁴ found that hemorrhage had been reported in 703 other cases, thus raising the total to 2,151. Approximately one-third of the cases in which hemorrhage had been reported were assigned to other causes. At the same time, however, all the deaths in which infection was mentioned, were coded under that heading.

TABLE III. PUERPERAL MORTALITY, U. S., 1936

12,182 DEATHS

1398 assigned to hemorrhage	
703 additional	
1635 assigned to accidents of labor	
3000 additional, assigned to	
hemorrhage	811
infection	1034
toxemia	786
embolism	336

Janssen⁴ showed, too, that 1,635 cases were formally assigned to accidents of childbirth, yet there were more than 3,000 additional cases reporting complications of delivery which had been variously tabulated under a single cause. Of these 1,034 were assigned to infection, 786 to toxemia, 336 to embolism and sudden death, and 811 to hemorrhage. When one recalls that accidents of childbirth statistically include injury during delivery, lacerations, inertia and atony of the uterus, as well as inversion and rupture, malpresentation and position, dystocia, prolonged labor, instrumental delivery, cesarean section, version and obstetric shock, an obstetrician need not exercise his imagination to estimate the frequency and importance of hemorrhage in the large number of cases tabulated otherwise. Here particularly the entire problem of joint cause selection is so difficult, so nearly impossible, that statistical

deductions as to the relative frequency and importance of hemorrhage and infection may properly be questioned.

In Brooklyn, too, all the major causes of death have shown notable decline.⁶ During the five-year period 1937 to 1941, the number of deaths fell from 164 to 79, and the puerperal mortality rate was reduced from 4.0 to 1.6. On the face of these statistics, infection maintained its position as the leading cause of death.

TABLE IV. MAJOR CAUSES OF MATERNAL DEATH IN BROOKLYN, N. Y.

	1937	1938	1939	1940	1941	TOTAL
Total No. Deaths	164	135	110	111	79	599
Infection	30	27	30	22	12	121
Toxemia	26	18	12	17	8	81
Hemorrhage	21	24	13	11	12	81
No. of Births (in thousands)	40.3	40.3	40.3	42.1	48.3	

The downward trend was well maintained for all three principal causes of mortality. However, not all the causes were reported on the certificates of death; neither infection nor toxemia was forgotten or ignored, but very often hemorrhage was not mentioned or, if reported, was considered only as an associated cause by the vital statisticians and so not tabulated. In 1940, for example, the number of deaths from hemorrhage appeared to be but 11, but there were 17 additional deaths in which hemorrhage was coded as a secondary cause. Statistical precedence had been given to infection in 4 cases, toxemia 2 cases, cesarean section 3 cases, embolism 1 case and abortion 3 cases. And in the lists of deaths associated with pregnancy but assigned to nonpuerperal causes, 4 more cases of hemorrhage were found. They are of interest.

1. Streptococcal pneumonia associated with placenta previa which caused repeated and profuse hemorrhage. Delivery was effected by Pinard maneuver.

2. Hemorrhage and shock following induced incomplete abortion associated with rheumatic heart disease.

3, 4. Two women with syphilis who died of hemorrhage and shock, one after post-partum hemorrhage, and the other after rupture of uterus.

In every one of these 17 cases, hemorrhage was profuse, and in many the actual cause of death.

When certificates of death were compared with actual case reports submitted to the Committee on Maternal Welfare of the Medical Society of the County of Kings, it was found that neither infection nor toxemia had failed of report. Hemorrhage, however, had often been omitted, and even when reported as an important contributory factor, had disappeared under joint cause rules. If 37 deaths directly due to hemorrhage and shock, but assigned otherwise, are added to the hemorrhage factor, and proper corrections are made elsewhere, hemorrhage appears as the most frequent cause of maternal death.

TABLE V. MAJOR CAUSES OF MATERNAL DEATH
(REVISED)

	1937	1938	1939	1940	1941	TOTAL
Infection	27	27	30	18	10	112
Toxemia	26	18	12	10	8	74
Hemorrhage	29	27	14	28	20	118

If the figures are further revised so as to include 9 additional cases, in which hemorrhage was known to be profuse or repeated, yet not the actual cause of death, the importance of hemorrhage and its failure to yield to preventive measures becomes even more apparent. And, if it is accepted that the principal purpose of tabulating the causes of maternal death is to plan and accomplish their prevention, then the deaths assigned to accidents of childbirth might well be taken into account, as they are largely associated with, or directly due to, the trauma of delivery. Comparisons with years before 1940 are very difficult, but every effort has been made to make corrections in accordance with the 1940 revision of the International List of Causes of Death. If these deaths are included, after deducting those which were directly due to anesthesia, revision of the mortality trends easily shows hemorrhage as the principal cause of maternal death. (Table VI and Fig. 1.)

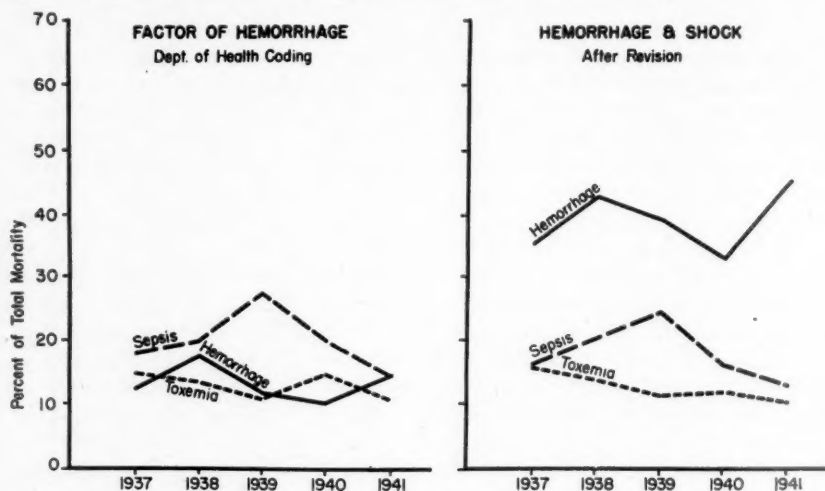


Fig. 1.

TABLE VI. MAJOR CAUSES OF MATERNAL DEATH
(FURTHER REVISION)

	1937	1938	1939	1940	1941	TOTAL
Infection	26	27	27	18	10	108
Toxemia	26	18	12	10	8	74
Hemorrhage	31	29	16	28	23	127
Acc't. Childbirth	29	29	27	8	13	106
Excluding Anesth.	60	58	43	36	36	233

In Brooklyn, hemorrhage is the most frequent cause of puerperal death, and so the most important. Certainly it is not expected that it will prove so in every locality, but it will in many. In Connecticut,⁷ for example, with 61 puerperal deaths in 1939 and its low rate of 2.6 per 1,000 live births, hemorrhage was responsible for the largest number. And in the City of Buffalo from 1935 to 1940, 20 per cent of the deaths were assigned to hemorrhage and 23 per cent to sepsis, yet this sepsis rate was greatly influenced by operative delivery, particularly cesarean section. The third largest group was not toxemia, but accidents of

pregnancy and labor, with a high incidence of pulmonary embolism in operative deliveries.

Through the courtesy of the Director of the Bureau of the Census⁹ it has been possible to discover the number of cases in which puerperal hemorrhage and puerperal septicemia were reported as secondary causes, and the number of deaths from these causes which were associated with other puerperal conditions. These figures have not as yet been published. In 1940, a total of 2,207 cases were assigned to infections during childbirth and the puerperium, and 1,037 to hemorrhage of childbirth and the puerperium. There were, however, 363 additional cases in which hemorrhage had been reported as a joint cause but which were tabulated otherwise, 226 of them were assigned to septicemia. And no less than 545 cases of embolism and sudden death which occurred during or after delivery were assigned to infection as well. To other accidents and specified conditions of childbirth, a title which includes laceration, rupture or other trauma of pelvic organs and tissue, and other conditions causing difficult delivery, 550 cases were assigned. There were, however, 1,385 cases in which these conditions had been reported; 456 were assigned to infection and 379 to hemorrhage. It is probable that if case reports were available for comparison with certificates of death, as they are in Brooklyn, the true frequency of hemorrhage would be discovered (Table VIII).

TABLE VIII. HEMORRHAGE AND INFECTION, U. S., 1940

Assigned to infection	2,207
to hemorrhage	1,037
to accidents of labor	550
to embolism and sudden death	545
Hemorrhage assigned otherwise (226 to infection)	363
Total Accidents of Labor	1,385
Assigned to infection	456
to hemorrhage	379
to accidents of labor	550

Comment

Hemorrhage has always been one of the major causes of obstetric death, yet it may be the most frequent cause, and at present it is the most important. Plass¹⁰ believes that "The reduction of the death rate from infection and toxemia by increased efficiency in prevention and treatment threatens to make hemorrhage and shock the leading cause of obstetric fatalities if they do not already occupy that unenviable position."

No doubt there is progressive increase in blood volume during pregnancy and particularly in the later months. And it is true that the parturient woman is often able to survive the loss of a large amount of blood. Yet it is exactly this impression or experience that is responsible for frequent failure to carry out thoughtful prophylaxis or to make adequate preparations for blood replacement. Hemorrhage cannot always be prevented, but the results of blood loss are largely controllable.

In abortion and ectopic pregnancy, hemorrhage is usually repeated before it becomes considerable. Vaginal examinations and long periods of trial of oxytocics are often followed by slow or inept removal of re-

tained tissue with free bleeding. It is common for patients to return to bed with evidence of severe blood loss in the operating room.

In Brooklyn, the placenta previa mortality has been largely due to procrastination. In no case did initial hemorrhage cause death. In 18 out of 26 cases, repeated hemorrhage occurred before any treatment was instituted, a week or more elapsing in 12 cases.

Thoughtless management of the third stage of labor invites postpartum hemorrhage. Blood loss from an episiotomy wound is rarely negligible, and may be considerable, while repair is going on under unduly prolonged anesthesia. The anesthesia itself, if ether or chloroform, may interfere with normal contraction and retraction after delivery of the placenta. Abdominal delivery, too, may be associated with unexpected and serious hemorrhage, particularly the classical operation.

Whether shock can be caused by uncomplicated hemorrhage, according to Blalock,¹¹ or cannot, according to Moon,¹² is of no importance in practical obstetrics, for it is certain that hemorrhage is a contributory factor of the utmost importance. Protracted labor with its wounds and pain, its fatigue and discouragement, its anxiety and fear and other emotional disturbances is the battlefield of obstetrics, and its casualties are not very different from those of war. Continuous and rapid dehydration by sweating and vomiting, or failure to replace lost body fluids must surely result in decreased blood volume, increased blood viscosity and capillary stasis. Even comparatively slight bleeding may be followed by death, and it is clear that operative pelvic delivery, with or without serious hemorrhage, is in no way comparable to carefully planned abdominal surgery.

Anesthesia makes a significant contribution. Not infrequently, administration of any anesthetic will bring about circulatory decompensation in those in whom shock is impending, but who appear to be in good condition. Ether and chloroform tend to increase blood loss. Satisfactory analgesia of nitrous oxide is associated with steadily increasing anoxia. Spinal anesthesia, if it has not affected the respiratory mechanism, invites shock by causing vasodilatation. Even analgesics in slow labors, which tend to increase the incidence of operative delivery, merit consideration. Chloral and barbiturates in large doses will increase capillary permeability.¹³ Even morphine tends to cause the anoxia which is so important in the causation of shock. And acidosis will follow well-developed anoxia. Local anesthesia, obviously, will have less general effect than any inhalation anesthetic.

It is not my purpose to examine all the conditions and circumstances which contribute to obstetric hemorrhage, nor to propose a detailed preventive program. Knowledge of methods of prevention is fundamental, and successful management of serious hemorrhage depends largely upon the skill of the obstetrician and timely replacement of lost blood. Hemorrhage cannot always be anticipated, but it is possible to be prepared for it. The implications are clear.

Circulatory efficiency can be maintained only by restoration of blood volume. Surely every physician knows that lost blood must be replaced by blood or a satisfactory substitute, yet, in practice undue confidence is had in almost everything else, and blood and plasma are by no means as widely used as they should be. It is obvious that the best method of treatment of shock involves its early recognition, but not every physician knows that even slight decline in the systolic pressure

is of great significance, and that low blood pressure is not an early symptom. Nor does every physician know that crystalloid solutions are ineffective if blood loss has been serious; that often only large amounts of blood will save life; and that preparations for transfusion from voluntary donors involve valuable loss of time; nor is everyone aware that infusion of plasma may be accelerated by the syringe, when time presses, or that the sternum may be used for administration of blood and plasma, by drip or syringe, when veins are collapsed.

Since citrated blood, because of its availability and ease of administration meets all the requirements of the obstetrician, blood banks are ideal, yet even they are not certain sources of supply even in the largest hospitals. A plasma bank is practical for even the smallest hospital, while a blood bank is not. And plasma, which any hospital may store near its delivery room, is commercially available, yet not every lying-in institution is aware that it must include blood or blood substitutes in its resources. Women cannot be expected to make this inquiry themselves. Perhaps, as a result of the war, a plasma conscious public will contribute blood to avert the casualties of obstetrics, through cooperation of the same agencies which are carrying on this work so well now.

In Brooklyn, hemorrhage is the outstanding controllable factor in puerperal mortality. Far more common everywhere than indicated by its statistical frequency, it has not yielded to preventive measures which can be clearly outlined. At present, hemorrhage is the most important cause of maternal death.

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THE INFLUENCE OF PREGNANCY ON THE LOCATION OF THE CENTER OF GRAVITY, POSTURAL STABILITY, AND BODY ALIGNMENT*

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ONE of the most rigorous demands made upon the human postural mechanism is that of pregnancy. For a period of 280 days the woman carries a steadily increasing load which at term averages, in totum, including uterus and ovum, 4 to 6 kilos (pounds 10-14). Mechanically, this load could scarcely be placed more disadvantageously. The low anterior position of the added weight limits joint adjustments and enhances the normal forwardly unbalancing gravitational stresses. Excessive postural realignments must be necessary to retain the center of gravity within the secure middle third of the supporting base. Further difficulties arise with the relaxation of ligaments and a loosening of the pelvic joints which have been shown to appear as early as the fourth month of pregnancy (Abramson et al., 1934,¹ Thoms, 1936).¹¹ It has seemed reasonable to presume that the low back pains which frequently accompany pregnancy, or develop as a sequel to it, might have an etiology, based in part, upon these disturbances in body mechanics.

Aside from studies made on weight changes and alterations in the pelvic joints few, if any, consecutive observations have been reported of the readjustments in body parts as they accrue in pregnancy and regress during the puerperium. Having available a cooperative subject trained in the laboratory procedures required, it seemed worth while to record the postural adjustments of the gravida by means of serial biplane photographs synchronized with center of gravity observations. The following paper presents the results of the study of the influence of pregnancy on the location of the center of gravity, postural stability, and body alignment.

Methods

The apparatus and procedure were essentially the same as that described by Hellebrandt and Kelso (1942).⁶ The subject (R. T. C.), a young secundigravida, aged 31, reported to the laboratory for nine observations, distributed in two-week intervals at the beginning and end of term. The following data were obtained for each of the experiments: weight in kilos and pounds, height of the center of gravity and the total height in recumbency, and kymogram records of postural stability during two minutes of comfortable standing with biplane profile and back view photographs taken every 15 seconds. Thus each experiment

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yielded a total of 18 photographs synchronized with center of gravity observations.

A planimetric average of the shifting gravity center for the single stance periods was calculated and projected into the footprints. Experimentally determined gravity lines were then erected into each photograph.

The initial record was made during the third month of pregnancy. The next two followed at the end of the first and at the beginning of the second trimester. No further observations were possible until the third trimester when biweekly experiments were resumed, the last one being performed ten days before delivery. A final observation was made six weeks after parturition.

Results and Their Interpretations

Table I presents a summary of the data recorded. Eccentricity is the per cent deviation of the experimentally determined center of gravity from the diameter passing through the geometric center of the supporting base in each of the two vertical orientation planes (Hellebrandt et al., 1937).⁷

1. *Height of the gravity center.*—The per cent height of the weight center is the ratio of the gravity height from the soles of the feet to the total recumbent height of the subject as measured by means of the gravity board developed in this laboratory (Hellebrandt et al., 1938).⁸ The range of the gravity height ratio for women is 53.00 per cent to 59.00 per cent. That of our subject at the end of the first trimester was 54.68 per cent, placing her within the lower quartile of the group of 464 normal young adult women studied by Hellebrandt et al. (1938).⁸ At the end of term the ratio had risen to 55.99 per cent to the score level of the upper quartile, representing a 2.40 per cent increase in the height of the gravitational center. This progressive increase in gravity height throughout pregnancy may be contrasted to the work reported by Okuyama (1933)¹⁰ who studied the gravity height changes in fourteen subjects at various times before pregnancy, and once during puerperium. He found no consistent rise in the weight center height and in some cases there was an ante-partum fall in the gravity center. The discrepancy may be explained by the difference in the methods used. Okuyama employed a device necessitating the raising of one end of the gravity board through a known angle. This procedure might well cause a displacement of the viscera and fetus and thus, explain the variation of his records as compared to those obtained on the simple gravity board used in our experiment, where the position of the subject was held constant.

2. *Eccentricity in the sagittal plane.*—The mean location of the center of gravity for each observation was projected into a single footprint of the subject (Fig. 1). The hollow circles show the proximity of the average location of the gravity center to the geometric center of the base during the first trimester when the total weight was approximately 65 kilos, and the eccentricity -2.00 per cent. The semi-solid circles indicate the posteriorly displaced gravitational center during the third trimester when the weight ranged from 73.75 kilos to 75.70 kilos. During this period the eccentricity varied from -5.10 per cent to -17.86 per cent. The greatest eccentricity was concomitant with the greatest weight increase (Table I).

TABLE I. SUMMARY OF DATA OBTAINED IN A STUDY OF THE INFLUENCE OF PREGNANCY ON BODY MECHANICS—SUBJ. R. T. C.

EXPERIMENT	ECCENTRICITY		WEIGHT KG.	HEIGHT OF CENTER OF GRAVITY PER CENT
	AP PER CENT	LAT PER CENT		
1	-2.65	-1.82	65.00	54.68
2	-2.01	-0.88	65.20	54.51
3	0.00	-3.19	67.10	54.63
3rd Trimester				
4	-5.10	-9.01	73.75	54.93
5	-11.12	-1.83	73.80	54.99
6	-5.58	-4.75	74.25	55.22
7	-17.86	-9.07	75.70	55.52
8	-12.05	-6.50	75.15	55.99
Post Partum				
9	+2.02	-5.11	65.00	54.56

+In front of the geometric center of the total base.

-In back or to the left of the geometric center of the total base.



Fig. 1.—Footprint showing the average location of the vertical projection of the center of gravity of R.T.C., for each two-minute observation made during pregnancy and puerperium.

The apparent direct relationship between weight increase and rise in center of gravity height with the backward deviations of the per cent eccentricity in the sagittal plane may be expressed numerically. The anteroposterior eccentricity was correlated by the rank difference method with the weight increase, giving a correlation coefficient of 0.83. Thus with an augmentation in the subject's weight, the vertical projection of the center of gravity moves closer to the ankle. Coincidental with the weight increase there is a rise in the gravity center in the horizontal plane. This, then, also shows a high correlation with the backward displacement of the center of weight and $r = 0.93$.

The puerperal resumption of the anterior position of the average gravity center is represented by the barred circle. The vertical projection of the center of gravity is approximately in its initial position close to the geometric center of the base with an eccentricity of only +2.00 per cent. The weight is again 65 kilos and the center of gravity height

lowered to 54.56 per cent as compared with the 54.68 per cent in the beginning of pregnancy. Thus, there is an almost exact return to original values of three factors: body weight, height of the center of gravity and stance eccentricity.

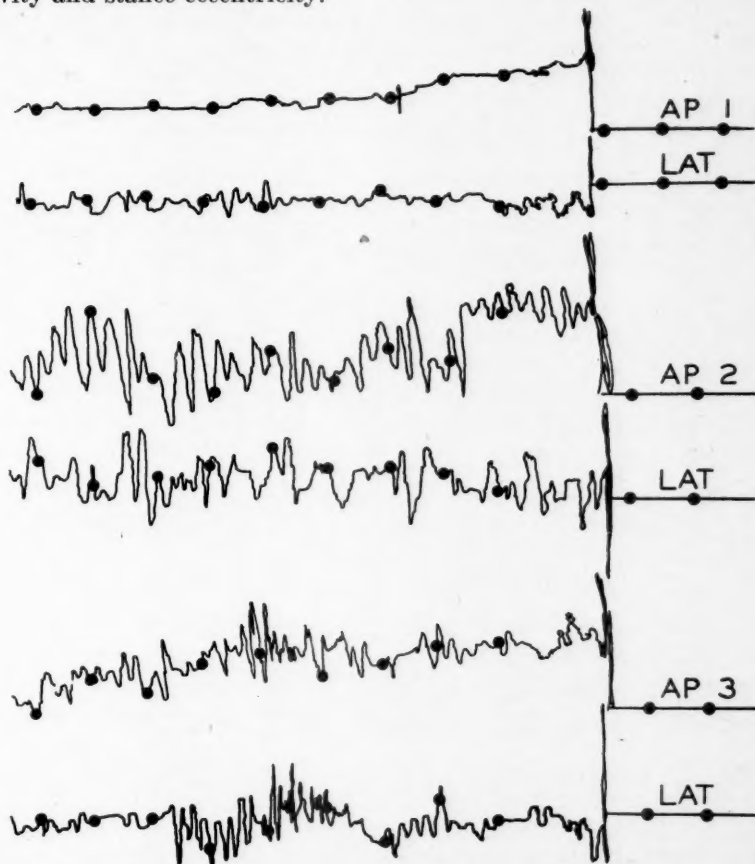


Fig. 2.—Kymograms of the shifting gravitational center of subject R.T.C. 1. First trimester; 2. Ten days ante partum; 3. Six weeks post partum.

3. *Location of the average center of gravity in the transverse plane.*—The planimetric averages of the shifts in the center of weight in the coronal plane do not vary more than 10 per cent. The subject stood with the weight slightly to the left of the geometric center of the base. This asymmetry has been demonstrated as occurring in approximately 80 per cent of all cases observed in this laboratory (Hellebrandt and co-workers, 1939-1942.^{3, 4} Apparently the added weight of pregnancy is so balanced that this fundamental asymmetrical stance pattern remains undisturbed in spite of the fact that the gravity center is displaced in the anteroposterior plane.

4. *Postural stability.*—A gross inspection of the kymograms of the shifting gravity center shows an increase in body sway throughout the period of pregnancy. One would expect such accruing instability to be associated with a rise in the height of the center of gravity and development of the fetal load. However, much of this sway was still present

post partum. Fig. 2 shows the anteroposterior and lateral records of the shifting center of weight. Apparently the initial degree of stability had not yet been reattained at the end of the puerperium. It is logical to assume, however, that, with the mechanical difficulties offered by the load and the loosening of the pelvic joints, the increase in sway during pregnancy is due to a decrease in postural stability which has a combined physical and organic basis. As it may involve a stretching of ligaments, postural stability is, perhaps, not as readily restored to pre-gravida conditions as are the other mechanical phenomena.

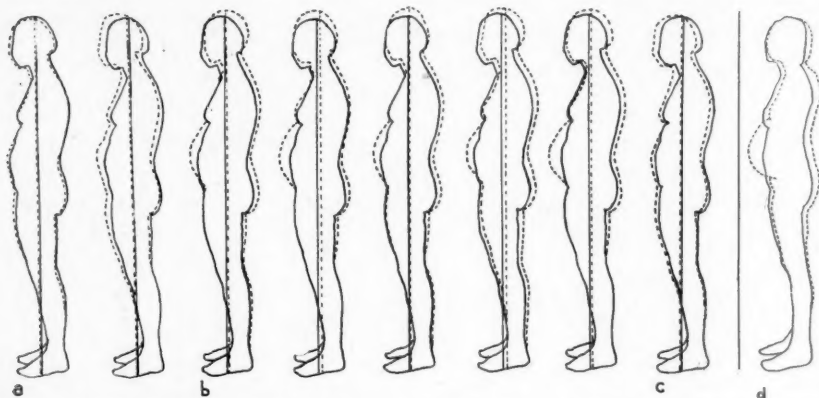


Fig. 3.—Tracings of superimposed photographs demonstrating the postural changes accompanying pregnancy.

"a," "b," and "c" Subject R.T.C. Successive observations (No. 2 through No. 9) are compared in turn (dotted line) with the photograph from experiment No. 1 (solid line) taken early in pregnancy.

"a." First trimestral series

"b." Third trimestral series

"c." Six weeks post partum

"d." Subject H.N. A photograph taken 24 hours ante partum (dotted line) is superimposed upon one of the same subject made 20 days after parturition.

5. Body alignment.—Changes in body contour and distribution of the segmented parts are demonstrated in Fig. 3. The solidly outlined figure represents the distribution of the body parts about the vertical projection of the center of gravity during the third month of pregnancy, at the time the first experiment was performed. Each successive observation is superimposed in turn upon this figure ("a" through "c") showing the gradual changes occurring throughout the ante-partum period with a rather striking return in the puerperium to the initial stance position. For comparison, observations made on a second subject (H. N.) of a much slighter build are included ("d").

The photographs of R. T. C. chosen for this study were those that most nearly approached the average location of the center of gravity in the sagittal plane during each period of observation.

Figs. "a" represent the stance at the end of the first trimester before any outstanding changes due to pregnancy have appeared. The head is forward. The upper back is well rounded and the knees relaxed. Figs. "b" are illustrations of the biweekly observations of the third trimester. A marked alteration in body contour may be noted. The gravity line moves backward. The head is raised, and the knees are stabilized. In Fig. "c," taken at the end of puerperium, the head has fallen forward, the back again is rounded, the knees relaxed and the gravity line resumes the original anterior position. This illustrates

the constancy of the stance of a normal individual (Hellebrandt⁴ and Fries, 1942).⁵

Parallel changes seem to occur in subject H. N. ("d"). The solid line is the outline of a photograph taken 20 days post partum. The dotted line shows the posture and appearance of the subject 24 hours prior to delivery.

In both subjects H. N. and R. T. C. there appears to be an unexpectedly slight change in the lumbar region of the spine. The curves in both cases appear almost parallel. In R. T. C. there is a suggestion of a sharpened lumbar curve and the apex of the angle may be slightly higher during the last months of pregnancy, suggesting some pelvic rotation. The data seem to indicate that the major counterbalancing adjustments are made by elevating the head, extending the cervical spine, stabilizing the knee joint, and leaning backward from the ankle.

Discussion

The results corroborate to a certain extent the accepted concept of postural changes in pregnancy (DeLee and Greenhill, 1943).² The upper back does appear to be straightened. However, analysis of the pictures seems to demonstrate little actual change in the dorsal spine per se. Instead, the straightening occurs primarily in the cervical region. Similarly the "exaggerated lumbar curve" commonly thought to occur, is not prominent in our subjects. One might surmise from these two cases that in certain individuals the upper body is retro-extended as a whole to counterbalance the increased forward load. Kerr and Lagen (1936)⁹ state that in pregnancy the head falls forward and the knees are bent and relaxed. Our experience seems to indicate that the adjustments are made entirely in the opposite direction, with a raised head and a stiffening of the knee joint.

It appears evident that with an increase in the anteriorly placed load the subject compensates by leaning backward beyond her normal gravitational center. This apparent "overcompensation" to a poorly placed weight which must be carried for a long period of time, can be contrasted to the comparatively slight disturbing influence of a much heavier load carried on the back. In this latter position, the added mass to the back acts as a counterweight to aid the subject in opposing the forwardly unbalancing gravitational forces. Furthermore, adjustments to a dorsal load are made by anterior body lean, with the degree of motion limited by the powerful antigravity muscles. The subject carrying a weight on the back can readily achieve an equitable balance between the added load and collapsing gravitational stresses and the center of weight remains essentially undisturbed (Hellebrandt, Fries and Larsen, 1942).⁵ In contrast, during pregnancy the added weight augments the normal forwardly unbalancing effects of gravity, and the controlling antagonistic muscular action is through the comparatively weak flexor groups. Thus, the position of the load and the resulting direction of the counterbalancing reactions make fine equilibratory ad-

justments difficult. However, the machine more than compensates. It widens the margin of safety anteriorly, and thus protects against an acute unbalancing force which might lead to a forward fall, endangering the fetus.

Summary

1. The anteriorly unbalancing load of pregnancy causes a temporary overcompensation which displaces, backward, the average location of the vertical projection of the center of gravity in the sagittal plane.
2. Pregnancy appears to be associated with no alteration in the subject's normal sinistral asymmetry of stance.
3. The multijointed segmented body counterbalances the disequilibrating effects of pregnancy by elevation of the head, hyperextension of the cervical spine and extension of the knee and ankle joints. Relatively slight visible adjustments occur in the lumbar spine.
4. There is an apparent significant decrease in postural stability which persists throughout the puerperium.
5. Since the alignment at the end of puerperium is an almost exact duplication of that assumed in the early months of pregnancy, the gravida has successfully resisted the chronic disrupting force without any significantly permanent change in the postural mechanism.

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THE SIGNIFICANCE OF THE ERYTHROCYTE SEDIMENTATION RATE IN PELVIC PATHOLOGY*

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THE erythrocyte sedimentation rate has been generally accepted as an aid in the diagnosis of infections and in the interpretation of normal and destructive processes. However, reports of the results of this simple test have been very conflicting. Two possible factors may be responsible; first, the nonspecificity of the test and secondly, the lack of uniformity in technique. A rapid sedimentation rate may not necessarily be due to a lipoma of the arm found coincidentally. Similarly, a limited physical examination invalidates the interpretation of the sedimentation rate. The test is not specific. The lack of uniformity in technique is due mainly to our ignorance of the mechanism underlying this phenomenon and adds further to the confusion.

From experimental^{2, 21} and clinical^{4, 18} observation, it has been found that the factors responsible for the sedimentation of erythrocytes are contained in the plasma. Cutler has shown that when the cells of slowly sedimenting blood were transferred to the plasma of rapidly sedimenting blood, they settled rapidly; whereas, when the cells of rapidly sedimenting blood were transferred to the plasma of slowly sedimenting blood, they settled slowly. The addition of lecithin, sodium oleate, bile salts or formaldehyde to rapidly settling blood, inhibited sedimentation; while the cells so treated when resuspended in "fast" plasma, again settled rapidly. The addition of acacia, agar, casein or gelatin to slowly settling blood increased the sedimentation.

Methods

There are three accepted methods of performing this test: (1) the Linzenmeyer method which determines the time required for a column of red blood cells to settle 18 mm.; (2) the Westergren method of recording the column of red cells after 15 to 30 minutes; one, two, six and twenty-four hours of settling; and (3) the Cutler graph method.³ Renwa¹⁵ stated that the Westergren method is most reliable because of the frequent intervals of recording. It would seem that the graph method would be even more reliable with readings recorded every five minutes for one-half hour, since the important phase of the sedimentation occurs in the first half-hour. The graph method, therefore, was used throughout this study.

Using a graph, the sedimentation of the erythrocytes in a 50 mm. column of citrated blood is interpreted thus: "A maximum settling in five minutes of 1 mm. or less, with the 1 mm. rate not repeated more

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than twice during the half-hour, is normal. Everything else is abnormal and therefore pathologic. Generally speaking, a maximum rate in 5 minutes of 1 mm. with the 1 mm. repeated three or more times during the half-hour, or rates between 1 and 4 mm., indicates disease of slight intensity; rates of 4 to 9 mm. indicate moderate intensity, and rates of 10 mm. or more, marked intensity." To facilitate recording, the normal graph is specified as reaction 0, that of slight intensity as reaction I, that of moderate intensity reaction II, and the curve of marked intensity as reaction III.

The three phases of sedimentation, i.e., formation of rouleaux, actual sedimentation of the aggregates and the packing of the red cells, become evident. An interpretation based on the maximum fall in millimeters in five seconds, is definitely more sensitive than an interpretation based on the fall in millimeters in one hour or on the time necessary for the red cells to fall eighteen millimeters since the latter two usually include all three phases.

A graph taken in case M. N. of epidermoid carcinoma, grade 3 of the cervix, League of Nation's classification stage 2, showed that the graph interpreted the line as reaction I, while the total fall of 10 mm. in one hour was on the borderline between normal and abnormal sedimentation.

Correction for anemia is misleading, as shown by Cutler, Park and Hess, Diggs and Bibbs,⁵ and Whitting and Miller.²¹ Anemia plays a part in the third phase and prolongs the second phase only by delaying packing. It is the pathologic condition with subsequent anemia that produces the rapid sedimentation, not the anemia per se. Both Cutler and Diggs reported normal sedimentation in severe anemia associated with sickle cell anemia. In this series of cases, one patient with recurrent anaplastic carcinoma of the ovaries in the terminal stage, had a hematocrit of 15 and a normal sedimentation rate. With the graph method, the packing phase does not affect the reading.

The actual conditions for the performance of the test in this study were set down as follows: (A) Blood should be taken either before a meal or at least two hours after eating. Recent investigation however⁷ does not substantiate the report of any increase in erythrocyte sedimentation rate after food. (B) The test must be performed within two hours after the blood is taken because there is frequently a decrease in the sedimentation rate after the blood has stood for 4 to 6 hours. (C) The Cutler sedimentation tube must be suspended in air to insure a vertical position as an inclination of 2.3 degrees gave a 30 per cent error in a 100 mm. length tube.²² This was readily accomplished by the use of an ordinary rubber stopper with a loop of thread passed through its center. (D) 0.5 c.c. of 3.8 per cent sodium citrate was used for every 5 c.c. of blood. The citrated blood was stored in a refrigerator at a temperature slightly above freezing. Any blood which showed evidence of clotting or hemolysis was discarded as unsuitable.

Results

Two hundred and nine tests were performed on 205 patients. Of these, one hundred and thirty-nine had benign lesions and sixty-six had malignant tumors. The benign lesions included infections, cysts, tumors and pregnancies. The malignant tumors included sixty-five cases of carcinoma of the genital tract and one case of myosarcoma of

the uterus. Repeated readings of seventy samples of blood were taken after six, and after twenty-four hours of standing in vitro.

Benign Pelvic Lesions

Bartholin cysts, relaxed perineal floor, cervicitis, malposition of the uterus and endometrial hyperplasia do not cause a rapid sedimentation rate. Bartholin abscess, lymphogranuloma venereum and ulcer of the cervix after cauterization cause a rapid sedimentation rate. Sedimentation rate does not help in differentiating a benign from a malignant ulcer of the cervix.

There were fifty-one cases of uterine fibroid. Forty-one or 80 per cent gave an erythrocyte sedimentation rate of reaction 0 or I_2 , i.e., reaction I with a maximum rate of 2 mm. per five minutes. Ten cases gave a reaction over I_2 . These ten patients were found either to have other pathologic conditions associated with the fibroma to account for the rapid rate, or developed serious complications postoperatively. In two cases, the fibroma was associated with pregnancy between the third and fourth months. One patient showed evidence of an old infected incomplete abortion. Another had tubercular appendicitis in addition to the uterine fibroma. Two patients developed bronchopneumonia and one a *B. coli* urinary infection. Two developed thrombosis and in one of these cases death followed a pulmonary embolus. In one patient there was nothing to account for the rapid sedimentation except that she had received a transfusion of 500 c.c. of whole blood the day before the test was performed. The relationship of rapid erythrocyte sedimentation to the subsequent development of complications is not clear.

Eighty per cent of all the patients with fibroma of the uterus not coincident with other pathologic conditions showed a normal or slightly rapid sedimentation rate. Those in whom the result was abnormal to the extent of reaction I_2 , gave evidence of hemorrhage, necrosis and calcification in the fibroid, although such degeneration did not invariably increase the sedimentation rate. Mathieu¹³ in his thirty-nine cases of uterine fibroma made the statement that a bleeding submucous fibroma causes rapid erythrocyte sedimentation. I could not confirm this finding. It may be questioned whether it was the degeneration and infection in the submucous fibroid that caused the increased rate, or a recent transfusion for combating the severe anemia was responsible. It can be stated that a normal sedimentation rate, or one of reaction I_2 , or less, is a safe indication for surgery in fibroma of the uterus. A patient showing an increased sedimentation rate of I_2 , or higher, warrants further study to determine the probable presence of some other pathologic or physiologic condition.

There were twenty-five cases of pregnancies in this series. Six were in the last trimester, five in the second and fourteen in the first. The sedimentation rate was found to be increased in all the patients in the second and third trimesters. These results agreed with those obtained from larger series of pregnant women.^{1, 20} The rate was found to be variable in the first trimester. It was increased in two of three non-infected intrauterine pregnancies in the third month, in two of four patients in the second month. Two patients with infected incomplete abortion showed a rapid sedimentation rate. There were five cases of ectopic pregnancy of less than two months' duration. Increased sedimentation rate occurred in two patients who had massive hemoperi-

toneum. However, in two with some free peritoneal blood, and one without bleeding, the rate was normal. Hemoperitoneum therefore, unless massive, does not cause an abnormal sedimentation rate. A rapid rate in a suspected ectopic pregnancy, unless there is clinical evidence of hemoperitoneum, is against such a diagnosis and urges consideration of an inflammatory process.

The use of the erythrocyte rate in the differential diagnosis of salpingitis and appendicitis has been repeatedly reported.¹⁰⁻¹⁹ There are conflicting reports regarding the rate in acute appendicitis, although most writers agree that salpinitis gives a much more rapid rate than appendicitis. Lesser and Goldberger reported a normal rate while Lintgen and Fry found an abnormal rate in 52 per cent of the patients with appendicitis without rupture, including catarrhal, suppurative and gangrenous appendicitis. Lesser and Goldberger used the Westergren technique while Lintgen and Fry used the graph method. The sedimentation rate in the two cases of purulent appendicitis included in this study gave reaction I, while that of a ruptured appendix with pelvic abscess reaction II, and all appendices considered as "chronic" had a normal sedimentation rate. There were six patients with inflammation of the adnexa. Three were diagnosed as fibroma pre-operatively, and laparotomy revealed a tuboovarian abscess and chronic salpingitis with sterile culture. The sedimentation rates ranged from reaction I to II. The other three were cases of acute salpingitis with sedimentation rates ranging from reaction II to III.

An explanation for the difference between the acceleration of the sedimentation rate in appendicitis and that in salpingitis has been suggested by Smith. He attributed it to the difference in the time of onset of symptoms. The Fallopian tubes, being more distensible, do not cause symptoms as readily as does the appendix. Therefore, inflammation has been established in the tubes for some time before causing symptoms, thus accounting for the higher sedimentation rate in salpingitis.

Among the ten benign ovarian tumors, which included parovarian cysts, pseudomucinous and serous cystadenoma and thecoma, the sedimentation rate was essentially normal except in those cases with complications. The five cases associated with rapid sedimentation rates were as follows: one had twisted pedicle, two were in the second trimester of pregnancy, one was associated with carcinoma of the breast, and the last case showed extensive necrosis and inflammation in the ovarian tumor.

Malignant Pelvic Tumors

There were three cases of squamous carcinoma of the vulva, grades 1 and 2. Two patients, showing evidence of groin metastases on admission, had been surgically treated. The third was treated by local caustic before admission and presented clinically an early lesion 1 cm. in diameter; microscopically the inguinal nodes presented no pathology. The sedimentation rate in the case of the last patient was normal while those of the first two gave reactions I and II respectively.

There were thirty-eight cases of epidermoid carcinoma of the cervix, five grade 3 and thirty-three grade 2, 8 per cent and 92 per cent respectively. Of these four were clinically classified as League of Nations stage 1, eleven stage 2, twelve stage 3, and three stage 4. Eight had been treated previously, therefore, it was not possible to classify them. All

TABLE I. CARCINOMA OF THE CERVIX

CLASSIFICATION	REACTION			
	I	II	III	NORMAL
L. of N. stage 1 (4 cases)	75%	25%	0	0
L. of N. stage 2 (11 cases)	91%	9%	0	0
L. of N. stage 3 (12 cases)	50%	50%	0	0
L. of N. stage 4 (8 cases)	33%	67%	0	0
Those treated elsewhere				
"No evidence of disease" (3 cases)	100%	0	0	0
"With evidence of disease" (5 cases)	20%	40%	40%	0

showed abnormal sedimentation rates varying from reaction I to III. The degree of rapidity depended partly on the extent of the disease, but more on the amount of infection present (Table I). This was brought out by the fact that reaction III occurred only after irradiation and one patient with this reaction had a left adnexal abscess as well. It is important to note that there were three patients, who had no evidence of the disease after being treated elsewhere, but still maintained an abnormal sedimentation rate.

There were thirteen cases of malignant lesions of the fundus uteri. Twelve were adenocarcinoma and one was myosarcoma. Eighteen per cent of the patients who applied for treatment were in the operable stage. The sedimentation rate was found to be increased in all cases.

Jacoby and Spotoft⁹ stated that 48 per cent of their ninety-one cases of uterine cancer had normal sedimentation rates. Seventy-one were cervical and twenty fundal in origin. This is in distinct contrast to the findings in this series in which only 3 per cent of the sixty-six patients with malignant lesions gave a normal sedimentation rate. However, the method used by these investigators was not given and 15 mm. was taken as their limit between normal and abnormal sedimentation rate. It might be presumed that it was 15 mm. fall of erythrocyte per hour. If the tubes were 100 mm. in length, the results might be comparable to the Cutler's 50 mm. tube, as length of the tube has been shown to affect the rate of fall.³ However, without uniform technique, it is difficult to compare the results.

Among the ovarian neoplasms, seven were malignant. There were four additional patients who had generalized abdominal carcinomatosis with ascites. The primary tumor cannot be definitely determined, either clinically or at post mortem, but most probably it was ovarian. Contrary to what might be expected, even in patients with ascites, the rapidity of the erythrocyte sedimentation rate was not remarkable. It ranged between reactions I and II only. One patient, No. 68462, with recurrent anaplastic carcinoma of the ovaries, with necrosis and hemorrhage, metastasis to the peritoneum with fibrinous peritonitis, paralytic ileus, ascites and pleural effusion, gave a normal sedimentation rate with a hematocrit of only 15. Wise and Durham²³ in their investigation of the sedimentation rate in Hodgkin's disease noted two cases showing normal sedimentation rate in the terminal stage. Gilligan and Earnstein⁸ in attempting to establish the relationship between the sedimentation rate and the fibrinogen content of plasma, mentioned one terminal case with severe liver damage which gave a sedimentation rate and fibrinogen content below the limit of normal. Cutler also observed a normal sedimentation rate in the terminal stage of tuberculosis. It is conceivable that in such patients, the factors most probably responsi-

ble for the rapid rate, the plasma proteins, have been greatly reduced because of the markedly diminished liver function.

On the whole, those patients with ovarian cancer, even with ascites, appeared more comfortable and had very little pain as contrasted with patients in a similar stage of cancer of the cervix. The clinical discomfort of the patient thus parallels the rapidity of the sedimentation rate. The cases of cancer of the cervix with reactions II and III were invariably associated with a great deal of infection. Reichel¹⁴ made the statement that the rate was not the reaction of the cancer, but rather the manifestation of resorption capacity for inflammatory and necrotic products. This emphasizes the importance of controlling infection for the greater comfort of patients with cancer of the cervix in the advanced stage of the disease.

Feldman⁶ reported 95 per cent maintenance of the sedimentation rate, *in vitro*, throughout twenty-four hours after withdrawal of blood in cases of malignant tumors and Hodgkin's disease in contrast to those with inflammatory processes whose rapid sedimentation rate showed a reduction toward normal after twenty-four hours. He advocated the additional observation of the sedimentation rate at the end of twenty-four hours as a means of differentiating malignant tumors from other conditions giving a rapid rate. In an attempt to corroborate his findings, fifty-one cases with malignant tumors and nineteen cases with inflammatory process, with rapid sedimentation rates, had repeated readings at the end of six, and twenty-four hours. In contrast to Feldman's findings, of the patients with malignant tumors, nineteen out of fifty-one (37 per cent) showed a decrease in the rate of sedimentation; and of the patients with inflammatory processes, only ten out of nineteen (53 per cent) showed a decrease. There is too little difference between the percentages in this series to give any significance to repeated sedimentation tests at the end of twenty-four hours. A possible explanation of the reduction in the rate after standing *in vitro* may be that irrespective of the cause of lesion, the less extensive it is, the greater the tendency towards a normal sedimentation rate. (Tables II and III.)

TABLE II. REDUCTION IN SEDIMENTATION RATE AT END OF 24 HOURS IN CARCINOMA OF THE CERVIX

L. of N. stage 1	75%
L. of N. stage 2	33%
L. of N. stage 3	16%
L. of N. stage 4	33%

TABLE III. REDUCTION IN SEDIMENTATION RATE AT END OF 24 HOURS IN INFLAMMATORY DISEASES*

Mild inflammatory processes (8 cases)	88%
Severe inflammatory diseases (11 cases)	27%

*Mild inflammatory diseases included lymphogranuloma venereum, salpingitis, etc. Severe inflammatory process included advanced tuberculosis with mixed infection.

After irradiation, the sedimentation rate may be temporarily increased, as observed by Madrazo¹² and Jacoby⁹ and in the few irradiated cases of carcinoma of the cervix included in this series. As a guide to prognosis, after the local lesion is well controlled, Jacoby and Spotoft stated that a normal sedimentation rate gave hope of a "cure" while a persistent rapid rate called for closer observation for recurrences.

Summary

Two hundred and nine erythrocyte sedimentation tests were performed on two hundred and five patients as a diagnostic aid in pelvic pathology. Of the two hundred and five patients, one hundred and thirty-nine had benign lesions and sixty-six had malignant tumors. Among the benign lesions, pregnancy and infection increased the sedimentation rate. Ninety-seven per cent of malignant tumors showed a rapid sedimentation rate. Persistence of the rapidity of the sedimentation rate at the end of twenty-four hours in vitro does not differentiate malignant tumors from inflammatory processes.

The test is a definite aid in differential diagnosis in pelvic pathology. As in nonspecific laboratory procedures, the result must be interpreted in conjunction with clinical history and findings. It is also important to have uniform technique before a comparison of results from various clinics can be made.

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PREGNANCY AND THE DOUBLE UTERUS

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LACK of fusion of the müllerian ducts, either complete or incomplete, presents to the obstetrician and gynecologist a problem which demands knowledge of the dangers which may result from this anomaly. Since the deformity occurs only once in about 1,500 obstetric, and about once in 2,000 gynecologic cases, it is probable that even the specialist may see but few cases in a lifetime.

Terminology

There is some confusion in naming the different degrees and types of the anomaly. All degrees of lack of fusion of the müllerian ducts exist, from notching of the uterus, as in uterus arcuatus, to two complete sets of genital organs. The uterus may be divided completely, or by a septum, and likewise the cervix and vagina may be partially or completely divided. Hence, the uterus alone, the uterus and vagina together, or the vagina alone may be affected. When the müllerian ducts fail to develop normally as well as fail to fuse, then one uterus or vagina, or both, become rudimentary organs. DeLee¹ lists nine variations as follows:

1. Uterus duplex bicornis cum vagina septa.
2. Uterus septus duplex or uterus bilocularis.
3. Uterus subseptus unicollis.
4. Uterus subseptus unicorporeus.
5. Uterus arcuatus.
6. Septate vagina.
7. Uterus bicornis unilaterale rudimentarius.
8. Uterus with closed accessory horn.
9. Uterus unicornis.

Graves² lists eight types which do not correspond in description or in terminology with the above. In any event, such terms do not immediately present a clear-cut picture and must be accompanied by a detailed description to be comprehensive. Such confusion could be avoided by a simplified classification, as:

1. Uterus arcuatus.
2. Double uterus with a single cervix.
3. Septate uterus with a single or a septate vagina.
4. Double uterus with a double cervix.
5. Uterus with a rudimentary horn or absence of one horn.

In this it will be noted that the terms "septate" and "uterus arcuatus" have been retained since they are in general use. The terms "bicornuate" and "uterus didelphys," frequently used interchangeably in the literature, are confusing and should be discarded. There are, of course, cases not covered by this proposed classification, but a few modifying words would be sufficient to denote variations.

Pregnancy in cases of double uterus is always an interesting phenomenon. The following cases are taken from the records of the New Haven Hospital and represent cases seen over a past ten-year period.

Case 1.—Pregnancy in a septate uterus with a septate vagina.

O. W., a 25-year-old primigravida, whose anomaly "double vagina and double uterus" was diagnosed correctly by her local physician. Difficulty during coitus was easily remedied without operation when the defect was explained to the couple. The patient was referred to the New Haven Hospital obstetric clinic when she became pregnant.

First seen on February 16, 1941, she gave her last menstrual period (L. M. P.) as October 8, 1941. History and physical examination were negative except for a history of severe dysmenorrhea. There was no history of pelvic anomalies in the family. Pelvic examination revealed a septate vagina; left side was somewhat smaller, both sides admitted two fingers without discomfort. Two separate, somewhat infantile, cervixes were demonstrated. The right cervix was softened and was the site of a small cervical polyp. On bimanual examination, it was felt that there were two separate uteri, the one on the left being normal in size, the one on the right being enlarged to the size of a two months' pregnancy, soft and boggy.

Roentgen pelvimetry revealed an essentially adequate pelvis. On February 28, 1942, the patient was admitted, having had cramps and vaginal bleeding for two hours prior to admission. Physical examination revealed the uterus on the right side to be the size of a 4 to 5 months' pregnancy. Fetal heart rate was normal, definite contractions were felt. Pelvic examination showed the bleeding coming from the nonpregnant side. Diagnosis, threatened abortion. The patient was kept under moderate sedation and was given progesterone for the next three days. The fetal heart rate remained good, while the slight vaginal bleeding and uterine cramps continued until March 2, 1942, when a uterine cast was expelled from the left uterus. The pathological report was "decidual cast with acute and chronic inflammatory reaction." When a basal metabolic rate was checked at -7, desiccated thyroid 0.06 Gm. a day was started along with wheat germ oil capsules. The patient was discharged on the sixth hospital day.

On March 26, 1942, the patient reported only slight spotting and slight cramps at rare intervals. Examination showed the nonpregnant uterus to be low in the pelvis on the left, and the fetus on the right to be presenting by vertex. On April 23, 1942, the fetus presented by the breech. Because of the danger of premature labor and in view of the patient's course, no attempt was made either to dislodge the nonpregnant uterus out of the pelvis or to do an external version.

On June 10, 1942 labor began. The fetus still presented by breech and the nonpregnant uterus remained incarcerated in the pelvis obstructing the birth canal. The cervix on the right was 1 to 2 cm. dilated. A low cervical type cesarean section was performed 7 hours after the onset of labor, the indication being incarceration of the nonpregnant uterus in the pelvis with breech presentation.

At operation the anomaly of the uterus was demonstrated to be a septate uterus with pregnancy in the right side. The nonpregnant side was low in the pelvis, the size of a 2 to 3 months' pregnancy. A 2,455 Gm. infant was delivered.

The postoperative course was uneventful and no additional tissue was passed from the left half of the uterus. The patient was discharged on her 14th day. At a subsequent visit the uterus was found to be well involuted and she reported that her menstrual periods were now practically painless.

During the past ten years at the New Haven Hospital obstetric admissions have totaled 9,822 and gynecologic 6,442. Nine cases, six obstetric and three gynecologic, of lack of fusion of the müllerian ducts were found; making the incidence of the anomaly about 1 in 1,500 obstetric, and 1 in 2,000 gynecologic patients. Abstracts of the remaining eight cases are presented here in abbreviated form.

Case 2.—M. E. J., a 41-year-old white primigravida married for one year, was examined first by her physician and told that she had a double uterus. History negative except for an appendectomy 20 years ago and removal of an ovarian cyst 14 years ago. In the fourth month of her pregnancy she passed a decidual cast from the right uterus with slight bleeding and cramps; during this time she was kept in bed for 4 to 5 days. In her sixth month she developed bronchopneumonia and was in the hospital for 9 days. Physical examination on admission at the time of labor was negative except for the pelvic examination, which revealed a vaginal septum with a separate uterus on each side, the left side being the pregnant side. A labor of 10 hours was concluded by low forceps after incision of the septum, which held up the head in the second stage. The baby weighed 7 pounds and 10 ounces.

Case 3.—M. C., a 30-year-old white para iii, gravida iv, was admitted October 10, 1941. Last menstrual period was given as July 16, 1941. She attempted abortion by medication, bleeding one day in August, September, and on October 8th passed some tissue; then spotted until admission to the hospital because of lower abdominal cramps. Physical examination was negative except for the pelvic, and evidence of rheumatic heart disease. Pelvic examination showed the cervix to be normal, some perineal relaxation, the fundus to be in midposition with a mass in the right adnexal region estimated at 8 to 10 cm. across, soft and fluctuant. The left adnexal region was negative. The preoperative diagnosis was question of abortion, complete, with right ovarian cyst or an ectopic pregnancy. At operation the patient was found to have a bicornuate uterus with pregnancy in the right horn, but the specimen had been nearly removed before the operator recognized the anomaly. Subtotal hysterectomy was performed. The pathological report was "bicornuate uterus with pregnancy in the right horn, normal endometrium in the left horn (no decidua)." (By the time the specimen had been removed there was partial separation of the placenta. We shall never know whether all the bleeding occurred from the passage of the decidua from the nonpregnant horn, or whether the operator was dealing also with an inevitable abortion.)

Case 4.—R. D. G., a 21-year-old white primigravida, had an incomplete double vagina and a double uterus with pregnancy on the right side. At operation the left side was slightly larger than a normal nonpregnant uterus. Cesarean section was done followed by a supravaginal hysterectomy.

Case 5.—Baby W., a premature of 1,965 Gm., was born with multiple defects, including a "uterus bicornis and a bifid vagina." Death occurred after 22 hours.

Case 6.—E. T., a 26-year-old white para 0, gravida iii, was seen with her third abortion at 3 months and was examined during her clinic visits by five different doctors; however, no one discovered the anomaly. It was not until the examination under anesthesia that the diagnosis of "uterus didelphys" was made. The patient had a double vagina, double cervix, and double uterus with the pregnancy and incomplete abortion being on the left.

Case 7.—J. K., a 46-year-old white nullipara, married for one year, was admitted with the complaint of dyspareunia. Pelvic examination showed a double vagina, both sides inadequate for coitus, two cervixes and two uteri. The septum was excised with relief of symptoms.

Case 8.—E. C., a 29-year-old para ii, had her first baby in 1939, at which time a diagnosis of "uterus didelphys" was made. Two cervixes were described in the history. Pregnancy, resulting in a 2,665 Gm. female infant, was complicated by mild pre-eclampsia. The patient had a spontaneous delivery after a labor of only two hours.

In 1942, with her second pregnancy, toxemia recurred in the eighth month. Pelvic examination showed vestiges of a vaginal septum and some irregularity of the fundus, at that time 2 to 3 months pregnant, which suggested a "bicornuate uterus." After a two-and-one-half-hour labor the patient was again delivered spontaneously of a 2,605 Gm. female. Diagnosis again recorded as "uterus didelphys."

To clear up the diagnosis, the patient was sent for, and vaginal examination revealed the second examiner to be essentially correct. A vestige of a vaginal septum was found in the vaginal vault, a single cervix and a "bicornuate uterus," each horn being easily demonstrated with a sound.

Case 9.—C. W., an 18-year-old white single girl, was admitted twice for pyelonephritis complicated by the absence of the left kidney. During the second admission a D. & C. done for menorrhagia revealed hyperplasia of the endometrium, a double cervix and a double uterus. On the third admission, a supravaginal hysterectomy was performed because of continued profuse uterine bleeding.

A review of the literature in recent years gives a total of 262 cases of these types of uterine anomaly. These may be summarized as follows:

Total cases	271
Obstetric	265
Gynecologic	6
Cesarean sections—total number	47
Corrected	41
Percentage—corrected	15.5%
Abdominal operations	
Obstetric—Exc. cesareans	8
Gynecologic	4
Incarceration of nonpregnant horn	12 or 4.5%
Maternal deaths	4 or 1.5%
Abortions—Smith, low quotation	12.8%
Schauffler, high quotation	53.0%
Average, DeLee and others	25.0%

Discussion

The diagnosis of congenital malformation of the female genital tract due to lack of fusion of the müllerian ducts is not usually made until

pregnancy takes place, although rarely dyspareunia is the presenting symptom. The condition is often overlooked and a patient may pass through pregnancy without difficulty. More often a pelvic mass is made out and the patient subjected to a laparotomy which may lead to the loss of all the pelvic organs, sometimes before the operator is aware that he is dealing with an anomaly and not a pathologic entity.

The presence of any vaginal anomaly should lead one to suspect further anomalies of the genital and possibly of the urinary tract. The exact type is often difficult to make out by means of bimanual palpation alone. Injection of a nonopaque medium, if the patient is not pregnant, will aid in determining the exact nature of the uterine lack of fusion. However, during pregnancy all the dangers of infection in a pregnant or pseudopregnant uterus, as in the nonpregnant horn, are encountered. When a rudimentary horn or vagina exists, the possibility of hematometra or hematocolpos is also present. As pointed out by Miller,³ regular menstruation does not rule out hematometra in a rudimentary horn.

Pregnancy.—The incidence of abortion in cases of uterine anomaly is about 25 per cent, although Findley,⁴ whose series numbered 135 cases, reported the somewhat higher incidence of 39.6 per cent. Schauffler⁵ found an incidence of 53 per cent. Since some cases of abortion may be due to an unrecognized anomaly, the higher figures may be more accurate. Premature labors are frequent, although no statistics on this point are available. A case reported by Oker-Blom, quoted by Findley,⁴ may shed light on the reason for the high incidence of abortion in these cases. This patient had a double uterus, one horn being smaller and poorly formed. Five pregnancies in the larger horn went to term, while four pregnancies in the smaller horn ended in abortions. Schauffler⁵ states that uterine septa and poorly vascularized irregularities of the fundus are responsible for the high incidence of abortions in these cases.

The anomaly has been reported by some writers as enhancing the chance of pregnancy, but Smith⁶ came to the conclusion that there was a decreased tendency, basing his statement upon a comparison of the average age of primigravidas and the length of time between marriage and pregnancy in his cases, as compared with controls.

Even after the danger from abortion has passed, the anomaly may still be a source of difficulty in pregnancy; such difficulty may vary from malposition of the fetus to rupture of the uterus. The latter, fortunately, has been rarely encountered.

Management in Pregnancy.—The proper management of the antenatal period and labor should be emphasized. Although in actual figures incarceration of the uterus occurred in only 4.5 per cent of the cases, one can read between the lines in many reports and question many more; especially when such reasons for cesarean section were

given as "failure of the head to descend" or "breech presentation." In early pregnancy, if the nonpregnant horn is palpated, it can be followed more easily during pregnancy as noted by Schauffler.⁵ In the case here reported in detail this was borne out. Findley⁴ states that, "in the event of delayed labor due to an impacted nongravid uterus that cannot be dislodged, cesarean section is indicated." Theoretically this is correct, but search of the literature fails to reveal any report of manual displacement at the time of labor. It might not be without risk due to the possibility of rupturing the uterus. Also, if the uterus failed to rise by itself, it probably would be impossible to raise it out of the pelvis after it had become moulded in place at term. If an attempt were to be made, it would seem that during the sixth or seventh month would be the best time. However, with the possibility of premature labor, that too seems ill-advised, and it is for just that reason that the author did not manipulate the uterus in the case here reported. Schauffler⁵ quotes others in the opinion that even though the uterus remains deep in the pelvis, it may not necessarily cause absolute dystocia or serious harm. In the case of a vertex presentation, which finally engaged after a trial labor, this statement may be agreed with, but in the case of breech presentation it would seem that cesarean section is absolutely indicated. Schauffler⁵ reports four breech presentations in his fifteen cases, but no incarceration of the nongravid uterus in any of these. Cesarean section was done because of the anomaly in 15.5 per cent of the cases collected, while eight additional cases had laparotomies for other reasons. This would seem at variance with the statement seen frequently in the literature that the management of pregnancy and labor in the double uterus should not differ from that of pregnancy in the normal uterus save in the event of complications. The condition itself is a complication of pregnancy and should be regarded as such. In Findley's⁴ series of 135 cases with a total of 217 deliveries, only 38.2 per cent of the deliveries were spontaneous while Falls⁷ reported major operative procedures in eleven out of fifteen cases. Any condition which results in as high as 53 per cent abortions, frequent premature labors, and then runs the gamut of operative obstetrics must be considered seriously. In handling these cases in labor it should be remembered that the cervix may be poorly formed, the musculature of the uterus may be irregular, poorly vascularized, thin and irregularly disposed while the stroma may be inadequate. A point particularly emphasized by Falls⁷ is that the fetal heart rate may become irregular during labor, probably on the basis of poor vascularization of the uterus, and this he considers an indication for cesarean section.

Third Stage of Labor.—In the event of spontaneous delivery the placenta often fails to separate, 37.9 per cent manual removals being reported by Smith.⁶ This may well be due to irregularities of contour, insertion of the placenta on a septum or faulty contraction of a poorly

formed fundus. In the event of spontaneous separation of the placenta, post-partum hemorrhage is not infrequent, Smith⁶ reporting 20 per cent in which uterine packing was necessary. Insertion of the placenta on an intrauterine septum or faulty arrangement of the musculature most certainly accounted for many of these hemorrhages.

Physiology.—Severe dysmenorrhea has been reported often in these cases. However, one of the most interesting problems is presented by the nonpregnant horn of the uterus and its decidua. Findley⁴ stresses the independence of function as evidenced by menstruation in the non-gravid uterus. Only one such case was found in the literature here reviewed. Schauffler⁵ reported bleeding in three of his cases in which the pregnancy was carried to term and consistently in those who aborted. It is conceivable that the three who bled and were carried to term were bleeding from the nonpregnant horn. DeLee¹ states that the decidual cast may be expelled and the pregnancy continue on the other side, but that usually it comes away in the puerperium. In the cases reviewed the matter was ignored except for a statement of Schauffler⁵ that "when bleeding occurs it should be considered as reflecting damage to chorionic tissue of the pregnancy itself and should call for measures combating threatened abortion." This is a reasonable attitude, but he further says that, "bleeding and bleeding with cramps are never to be regarded as harmless because it may be thought to originate in the accessory horn." The latter statement seems radical, for two out of the four cases in our small series of six cases in pregnancy had bleeding due to harmless passing of a decidual cast from the nonpregnant horn. The reason for the expulsion of the cast seems to be pressure from the expanding pregnant horn. This is the more plausible in those cases in which incarceration of the nonpregnant horn takes place. It is a matter of interest that apparently the decidua once expelled does not reform, for neither of our cases expelled decidua in the puerperium.

Morbidity and Mortality.—Maternal morbidity was reported by Smith⁶ as 30.7 per cent and was obviously due to the high percentage of operative deliveries. In the reported cases from the literature there were four maternal deaths, an incidence of 1.5 per cent. Fetal mortality was reported by Smith⁶ as 2.8 per cent corrected, 14.2 per cent uncorrected.

Conclusions

1. Duplication of the female genital tract due to lack of fusion of the müllerian ducts may be a formidable complication of pregnancy.
2. Simplification of the terminology in lack of fusion of the müllerian ducts seems necessary and a classification is here suggested.
3. Incarceration of the nonpregnant uterus with a breech presentation at term is an absolute indication for delivery by cesarean section.
4. Bleeding during gestation in a patient with duplication of the

uterus should be always carefully investigated. It may be due to passage of a decidual cast and not indicative of a threatened abortion.

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OBSERVATIONS ON THE ELDERLY PRIMIGRAVIDA

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THE presence in the hospital of an elderly primigravida is usually the cause of considerable anxiety to the attending physician, and doubts are frequently expressed as to the successful outcome of the pregnancy and labor. Are there valid reasons for the doubts and the anxiety?

In an effort to answer these questions, we have reviewed the records of primigravidas 35 years of age and over delivered at the Elizabeth Steel Magee Hospital during the five-year period between February 1, 1937, and February 1, 1942.

During this period there were 15,079 deliveries. One hundred and ninety-nine (1.32 per cent) were primigravidas 35 years of age and over. Most (108) of these were in the 35- to 36-year-old age group. Thirty-one patients were 40 or over, and of these the two oldest were 44 years of age. There were two sets of twins. Ward cases constitute approximately 50 per cent of all hospital patients, but only 17 (8.5 per cent), of whom seven were negroes, of the elderly primigravidas were of ward status. This is probably accounted for by the fact that most women in the lower economic bracket marry and beget offspring early. Therefore, the problem of the elderly primigravida is essentially that of the private physician and not the charity hospital.

The methods of delivery shown in Table I were employed.

TABLE I

Spontaneous	26	(13.2%)
Low forceps	86	(43.6%)
Midforceps	18	(9.1%)
Version and extraction	20	(10.2%)
Breech extraction	16	(8.1%)
Cesarean section	28	(14.2%)
Cesarean section with hysterectomy	3	(1.6%)
		(15.8%)

Not included are the two sets of twins. One set was delivered by breech extraction and version and extraction, and the other set spon-

taneously and by breech extraction. Dührssen's incisions were employed once and Piper forceps were applied to the aftercoming head in four instances.

When series of cases are published with a lower operative percentage than ours, yet with explanations and almost apologies on the part of the author for the incidence of operative procedures, we find it difficult to understand the rationale of these apologies. We have found, especially in the case of elderly primigravidas, that being "radical" early may be the most conservative procedure in the end. This hospital is almost exclusively limited to obstetrics and gynecology, and consultation is required for any suspected pathology or for any procedure other than low forceps. A better opportunity is thus offered for anticipation of difficulties than is present in most general hospitals. We are neither ultra-conservative nor radical, tending toward a middle-of-the-road policy, and we teach the medical students and resident staff accordingly. For the five-year period mentioned, cesarean section accounted for 4.54 per cent of all deliveries, version and extraction for 5.3 per cent, and spontaneous delivery for 55.22 per cent. We feel that elective cesarean section or version and extraction, while circumstances are ideal, is far better than to allow patients to have prolonged labors followed by difficult operative methods as a last resort. Only seven of the thirty-one sections in this series were in labor at the time of operation and none had prolonged labor with ruptured membranes. Obviously, version and extraction was performed while conditions were good since there was no instance of ruptured uterus. Many times it was used electively. It is easier and safer to stay out of trouble than to get out of it, once you are in. We acknowledge of course as a basic concept that the safety of the mother is paramount, but if, with this basic concept in mind, we feel we can also get a living baby, we do not hesitate to use operative procedures under ideal conditions. We do not offer excuses for the percentage of sections (15.8 per cent), or versions and extractions (10.2 per cent) in this series although almost 4 and 2 times greater, respectively, than the normal for all patients delivered in the hospital. Our results speak for themselves. With a woman of 35 or over, pregnant for the first time, the child is very important, and we frankly acknowledge that age may be the deciding factor in influencing us to resort to certain elective operative measures.

In analyzing the thirty-one cesarean sections, the indications were as shown in Table II.

TABLE II

Cephalopelvic disproportion	15	Chronic nephritis	1
Rheumatic heart disease	3	Coronary heart disease and fibroids	1
Degenerating or necrotic fibroids	3	Marginal placenta previa	1
"Elderly primipara"	2	Partial separation of the placenta	1
Quiescent pulmonary tuberculosis		Pre-eclampsia	1
with flat pelvis	1	Breech presentation	1
Tuberculosis of hip with naegle pelvis	1		

The factor of age came into play in at least nine of the sections done for disproportion, clinical judgment being placed ahead of x-ray evidence in four cases. As regards many of the other indications, the age of the patient was the deciding factor. Vaginal delivery might have been attempted had the patient been much younger. The opportunity to sterilize (4 cases) and perform myomectomy (1 case) was an added although not a deciding influence. Cesarean section followed by hysterectomy was performed in three cases, not due to prolonged labor and misjudgment of the size of the pelvis, but for necrotic fibroids in two instances and coronary heart disease with intramural uterine fibroids in the third case.

Turning now to the complications (Tables III, IV and V) found in the elderly primigravidas, one is astounded at their number and scope. The diseases of middle age have appeared. The friability and inelasticity of the tissues is evident. Such conditions are truly proof that the elderly primigravida warrants unusual care and attention.

TABLE III. COMPLICATIONS OF PREGNANCY

Premature labor at 5½ to 7 months	7
Fibroids	14
Essential hypertension	3
Nephritic toxemia	7
Eclampsia	3
Pre-eclampsia	9
Hyperemesis	4
Hydramnios	1
Rheumatic heart disease	3
Coronary heart disease	2
Pyelitis	3
Tuberculosis (hip, pulmonary)	2
Pneumonia	1
Syphilis	2

TABLE IV. COMPLICATIONS OF LABOR

Uterine inertia	34
Cervical stenosis	3
Partial separation of placenta	4
Marginal placenta previa	2
Prolapsed cord	3
Amnionitis	1
Retained placenta	1
Postpartum hemorrhage	5
1° Laceration of perineum	11
2° Laceration of perineum	12
3° Laceration of perineum	11
Complete	5
Sphincter fibers	6

The large increase in the number of complications of pregnancy in this age group over the usual run of obstetric cases is self-evident. Fibroids in fourteen patients, toxemias early or late in twenty-three patients, heart disease in five patients, all occurring in a series numbering only 199! Five per cent of the elderly primigravidas in this series either went into labor spontaneously and delivered before the fetus weighed more than 1,300 grams, which can be considered below the age of "viability," or were induced for maternal indications. There were seven cases of spontaneous premature labor at 5½ to 7 months' gestation, and three other patients had labor induced at this stage because of eclampsia, nephritic toxemia and intrauterine fetal death respectively.

In analyzing the complications of labor (Table IV), inertia and third-degree lacerations stand out. On reviewing the length of labor, it was found that the average for the 168 patients with vaginal deliveries was 17.4 hours. The shortest labor lasted 2 hours and 8 minutes, the longest 105 hours. Although only thirty-four instances of inertia are recorded among the complications, forty-nine patients (29 per cent) had labors of more than 18 hours, generally considered to be the average in a primigravida.

There were eleven third-degree lacerations of the perineum, despite episiotomies in most instances, which demonstrates how age increases the friability of the tissues. Midline episiotomy is not to be recommended in the elderly primigavida, but rather deep posterolateral incision. There were only 13 intact perineums following the 168 vaginal deliveries.

The postpartum complications (Table V) appear normal.

TABLE V. COMPLICATIONS OF PUERPERIUM

Lochiometra	3
Endometritis	3
Pyelitis	2
Pyelonephritis	1
Thrombophlebitis	1
Lobar pneumonia	1
Mastitis	1
Parotitis	1
Rectovaginal fistula	1

The average postpartum hospital stay was but 14 days, the shortest being 9 days and the longest 66 days—the latter due to thrombophlebitis. Only eight patients were hospitalized for 20 days or over following delivery.

An analysis of morbidity in accordance with the classification of Ziegler and Austin,¹ i.e.,

(1) Afebrile Zone—99° F and under

(2) First Febrile Zone—above 99° F and below 100.4° F

(3) Second Febrile Zone—100.4° F and above for 2 consecutive days excluding the first 24 hours, gives us the following:

There were 84 (42.21 per cent) afebrile patients; 84 (42.21 per cent) in the first febrile zone and 31 (15.58 per cent) in the second. This compares with the Elizabeth Steel Magee figures for the year 1937 of 48.47 per cent, 42.37 per cent, and 9.16 per cent respectively, as cited by Ziegler.¹

What of the infants of these elderly primigravidas? Males predominated in the ratio of 108 to 89 (plus 2 sets of male twins) and in patients over 40, the ratio was 18 to 13. The weights varied from 700 grams to 4,945 grams. There were 26 premature infants which weighed less than 2,500 grams. Ten infants weighed 4,000 grams or over. Only three infants presented abnormalities. These deformities were talipes equinovarus, talipes equinovaglus, and hemimelia.

In the final analysis, maternal and fetal mortality is the measuring stick of any method of handling a group of patients. Recently Wahrsinger and Kushner² reported a series of one hundred eleven patients with a maternal mortality of 2.7 per cent and a gross fetal mortality of 9 per cent. They cite a report presented by Nixon with 4 per cent and 17 per cent for the respective mortalities although no sections were done, as well as a report by Linden with no maternal mortality but 4 per cent craniotomies. In our series no mother died, but nineteen infants were lost, a gross fetal mortality of 9.5 per cent. As stated above, ten infants can be classified as "nonviable" due to the period of gestation and four others were macerated (the mothers of three of these were aged 41 years or over, and one had a section and hysterectomy for a necrotic fibroid, fetal heart sounds being absent prior to operation). The corrected fetal mortality is therefore 2.7 per cent. Of the remaining five infants, two were premature, weighing 1,925 and 1,975 grams re-

spectively; in the latter, the mother had labor induced for severe pre-eclampsia. The infant was stillborn. Of the three full-term babies, one, following low forceps delivery, died on the third day due to a tentorial tear; a second was stillborn following a difficult version and extraction, probably from the same cause; and the third died of hemorrhagic disease of the newborn on the third day after birth. It was delivered by midforceps because of maternal eclampsia.

Conclusions

A series of 199 elderly primigravidas delivered over a five-year period at a teaching maternity hospital is reported. This group comprises 1.32 per cent of total deliveries. There was no maternal mortality, a gross fetal mortality of 9.5 per cent, and a corrected fetal mortality of 2.7 per cent.

The elderly primigravida 35 years of age or over, is more subject to:

- (1) Loss of the fetus at 5 to 7 months—before "viability"
- (2) Premature labor
- (3) Degenerative diseases
- (4) Early or late toxemias of pregnancy
- (5) Inertial labors
- (6) Third-degree lacerations

With these complications in mind, more careful attention is needed to continue the pregnancy and more elective obstetric procedures may be needed at term to effect delivery. It is important, if operative interference is deemed necessary, that it be instituted as early in labor as feasible before the ideal time, as regards the safety of mother and infant, has passed. Individualization of patients is an absolute necessity.

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THE LOCAL USE OF ACID MEDIA AND SULFA DRUGS IN THE MANAGEMENT OF CERVICITIS AND VAGINITIS

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FROM 1936 to 1940 the local use of anhydrous lactose as a pH factor was studied and reported.¹ This anhydrous sugar applied as a vaginal pack produced buffered acids through bacterial decomposition encouraging the acid flora, Döderlein bacilli and inhibiting the pyogenic cocci by creating an environment pH 4.5.

It remained to be seen if by adding local sulfa drugs, further differential action could be obtained. Sulfa drugs are neutralized by the para-aminobenzoic acid present in pus.² Therefore, when pus is found in the cervix and vagina, a large concentration of sulfathiazole or sulfanilamide is needed locally to produce any bacteriostatic effect. Such factors as surface tension adhesiveness, and confining ability of the media were found to be of great importance when sulfa drugs were added. Contact of the sulfa drug with the surface lesion must be maintained constantly to be effective.

Sulfathiazole showed no clinical evidence of absorption from either cervix or vagina. One patient, who had a dilatation and curettage as well as an extensive conization of the cervix, had 30 grams of sulfathiazole powder packed into the cervix and vagina. Subsequent blood level concentration showed 0.3 mg. per cent. Another patient under identical conditions had 30 grams of sulfanilamide packed into the cervix and vagina, and showed a blood level concentration of 0.7 mg. per cent.

Sodium sulfathiazole, the sodium salt of sulfathiazole with a pH 9.6 to 12.0, caused sloughing of the cervical mucosa in ten cases and cervical erosion in twelve patients and could not be used alone. When combined with an acid medium or acid vehicle, it became sulfathiazole, losing its sodium ion.

Methods of application of sulfa drugs alone and in suitable vehicles have had our attention for the past two and a half years. Sulfanilamide is less effective in cervical and vaginal nonspecific infections than sulfathiazole. Sulfathiazole is also specific for the gonococci.

Conization of the cervix is the method of choice in removing cervical tissue containing nabothian cysts and infected glands.³ The remaining cervical tissue must recover from the burn inflicted at the time of conization. The effect of sulfa drugs in burns is well established.⁴

Sulfa drugs used alone in the vagina did not encourage the growth of acid vaginal flora, or retard the Döderlein bacilli in any way, if sugar or buffered acid jellies were also used. When sulfathiazole was mixed with beta lactose as a powder, insufficient concentration or

application of the sulfa drug resulted, and little or no improvement was noted over the use of the sugar alone for conization or vaginitis application. But when sulfathiazole was used alone as a cervical pack and filled the newly coned area of the cervix, and when such a sulfa pack was held in and against the cervix by a vaginal pack of beta lactose, marked clinical improvement in the rate and character of cervical healing after conization was noted in all cases. This procedure was done as a routine on all conizations, and the cervix cleaned and repacked with sulfathiazole and the vagina with beta lactose two times a week for the first two weeks postconization.

At the American Congress on Obstetrics and Gynecology in St. Louis, April, 1942, Dr. Dudley Smith and the author presented a scientific exhibit on the use of sulfathiazole at the time and following conization of the cervix and coagulation of Skene's ducts in selected cases of acute gonorrhea, which did not respond to oral administration of sulfathiazole.⁵ Twelve such patients who had received one gram of sulfathiazole four times a day for five days, for two or more such courses of therapy, still persisted in positive urethral and cervical cultures, and were subjected to conization of cervix and destruction bilaterally of Skene's ducts by surgical diathermy. Local sulfathiazole was used as in Table I on eight cases, and on four cases with buffered acid jelly, as shown in Table II. There was no morbidity noted in this rather radical procedure and eleven cases became free from the gonococci as demonstrated by repeated cultures. Only one patient later developed a positive urethral and cervical culture; she had had insufficient removal of cervical tissue at the time of conization. No greater test could be used to prove the effectiveness of sulfathiazole and a buffered acid medium of pH 4.5.

Since May, 1942, all cases of cervicitis and vaginitis, as well as pre-operative and postoperative conizations, have had buffered acid jelly applied as the vehicle for sulfa drugs. The formulas were as follows:

Sulfonamide Jelly (Gyn.), No. 151-3-B-2

200 mesh sulfanilamide	5.0%
200 mesh sulfathiazole	5.0%
Tragacanth flakes	3.0%
Granular boric acid	3.0%
Glycerin	10.40%
Powdered acacia	2.0%
Potassium hydroxide solution 18.8%	
4.5 c.c.	
Water	100.0%
to	
pH adjusted to 4.0 with acetic acid	

Sulfonamide Jelly (Gyn.), No. 151-3-B-4

200 mesh sulfanilamide	10.00%
200 mesh sulfathiazole	10.00%
Tragacanth flakes	3.00%
Granular boric acid	3.00%
Glycerin	10.00%
Powdered acacia	2.00%
Potassium hydroxide solution 18.8%	
Distilled water	100.00%
to	

pH 4.5 (actually 4.42)—adjusted with acetic acid

TABLE I. CERVICAL CONIZATION FOLLOWED BY SULFATHIAZOLE* PACK

DESCRIPTION OF POSTOPERATIVE CERVIX HEALING PROCESS IN WEEKS	BLEEDING MILD	AVERAGE AGE		AVERAGE PARA	DESCRIPTION OF CERVICAL LESION PREOPERATIVELY			
		PRIMARY	HEMORRHAGE		TYPE OF VAGINAL SMEAR	VAGINAL pH	CERVICAL pH	
			SECONDARY					
1. 74 cases, gray membrane and slough	10 cases	1 case		3	32 Old chronic cystic cervicitis			
2. 70 cases, gray membrane and slough	8 cases				22 Erosion, papillary with cystic change			
3. 40 cases, granulation clean	1 case				20 Laceration with erosion early cystic change			
4. 50 cases, granulation clean with epithelization be- ginning			2 cases					
5. 70 cases, epithelization, complete								
6. 73 cases, epithelization, complete								
7. 74 cases, epithelization, complete								
8. No stenosis, but cervical canal dilated								

*Winthrop Chemical Company, Inc., furnished the sulfathiazole powder for this series.

TABLE II. CONIZATION FOLLOWED BY SULFA DRUG IN ACID JELLY*

Weeks—	DESCRIPTION OF POSTOPERATIVE CERVIX HEALING PROCESS IN WEEKS	BLEEDING MILD	HEMORRHAGE		TYPE OF VAGINAL SMEAR	VAGINAL pH	CERVICAL pH	Average pH with nitrazine paper
			PRIMARY	SECONDARY				
1.	38 cases, gray membrane	2 cases	1 case		Type III	pH 6.0	pH 6.0	
2.	16 cases, gray membrane and slough	2 cases			Type II	pH 6.0	pH 6.0	
3.	30 cases, granulation clean with epithelization beginning				Type II	pH 5.0	pH 7.0	
4.	37 cases, epithelization, complete			1 case	Type I	pH 4.5	pH 7.0	
5.	38 cases, epithelization, complete				Type I	pH 4.5	pH 7.5	
6.								
7.	No stenosis							
8.								

*Ortho Products, Inc., furnished material using: 151-3-B-2 Sulfia Jelly 10% (5% each of sulfathiazole and sulfanilamide), pH 4.0; using 151-3-B-4 Sulfia Jelly 20% (10% each of sulfathiazole and sulfanilamide), pH 4.5. Ten of the 38 patients had 10% sulfia jelly, 28 cases had 20% sulfia jelly used throughout, ten of the 16 cases which had gray membrane and slough at two weeks, had been on 151-3-B-2 (10% sulfia jelly) and the remaining six cases were treated with 151-3-B-4 (sulfia jelly 20%).

TABLE III. CONIZATION FOLLOWED BY ACID JELLY.

	DESCRIPTION OF POSTOPERATIVE CERVIX HEALING PROCESS IN WEEKS	BLEEDING MILD	AVERAGE AGE		AVERAGE PARA		DESCRIPTION OF CERVICAL LESION PREOPERATIVELY		
			PRIMARY	SECONDARY	HEMORRHAGE	TYPE OF VAGINAL SMEAR	VAGINAL pH	CERVICAL pH	Average pH with nitrazine paper
1.	6 cases, gray membrane and slough with odor	2 cases				Type III	pH 7.0	pH 7.0	
2.	6 cases, gray membrane and slough with odor	2 cases				Type III	pH 6.0	pH 8.0	
3.	6 cases, granulation and slough	1 case				Type III	pH 6.0	pH 8.0	
4.	4 cases, granulation clean					Type III	pH 6.0	pH 8.0	
5.	3 cases, epithelization, complete					Type II	pH 5.5	pH 7.0	
6.	4 cases, epithelization, complete					Type II	pH 5.5	pH 8.0	
7.	6 cases, epithelization, complete					Type I	pH 5.0	pH 8.0	
8.	1 case of stenosis								

*Ortho Products, Inc., furnished the acid jelly base 151-3-B-3, pH 4.5.

Formula: Tragacanth flakes 3.0%
Boric acid granular 3.0%
Glycerin 10.40%

Acacia 2.0%
Distilled water 71.4%
Potassium hydroxide solution 18.8%

pH adjusted with acetic acid.

A routine in the cervicitis clinic is to apply with vaginal applicator mixtures of sulfathiazole and sulfanilamide in buffered acid jelly pre-operatively, at the time of conization, and postoperatively. Usual instructions to the patient are nightly vaginal applications of the jelly (5 to 10 c.c.) for the first two weeks, then every other night for the next two weeks, even though the patient were menstruating. Nightly applications during any period of bleeding or regular menses were insisted upon. Douches are prohibited, and intercourse forbidden. Table II summarizes thirty-eight cases of conization so treated with the above formulas.

The mechanical adhesiveness, yet free flow and capillarity of the jelly is necessary if the sulfa drug is to be efficiently applied to the cervix and vagina in this water soluble medium. The jelly flows into the conical area of the cervix and bathes the coned surface with the thick creamy sulfa drug and thus maintains closer application than was possible when the sulfa drugs were applied as a powder by blower, and the anhydrous sugar applied as a vaginal pack to hold it in place in the vaginal vault. The buffered acid jelly with the sulfa drugs has the additional advantage of patient self-application by means of a vaginal applicator. Clinical results show a marked improvement over any previous method studied.

When conization of the cervix has removed the disease-gland-bearing area of the cervix and the latter is healed, the vaginitis will be under control, and in most cases the patient will remain symptom-free from pyogenic infections of the vagina, if there is a normal estrogenic type of vaginal mucosa.

Vaginitis Study

There were patients with minor cervical erosion in which no morbid anatomy of the cervix existed, yet vaginitis was present. By definition there are three types of vaginal smears as follows:⁶

Type I, pH 4.0 to 5.0, Döderlein bacilli in abundant vaginal epithelium (desquamated)

Type II, pH 4.7 to 6.0, few Döderlein bacilli, few vaginal epithelial cells, trichomonads and few pyogenic organisms.

Type III, pH 5.6 to 8.0, no Döderlein[®] bacilli, no vaginal-epithelial cells, many cocci, colon bacilli, or other pyogenic organisms, not monilia.

These patients were grouped and treated as follows:

Twenty-eight cases received buffered acid jelly applied with vaginal applicator nightly for two weeks, then every other night for two weeks. (Fifteen per cent failure.) The formulas for this jelly are:

Glycerin	10.00%
Vegetable gum	5.00%
Boric acid	3.00%
Ricinoleic acid	0.75%
Propyl ester of parahydroxybenzoic acid	0.05%
Oxyquinoline sulphate	0.025%
Perfume	0.05%
Water to	100.00%

pH adjusted with acetic acid to 4.5

Fifteen cases (with 12 per cent failure) received 10 per cent sulfa jelly (formula 151-3-B-2) used as above.

Eighteen received 20 per cent sulfa jelly (formula 151-3-B-4) applied with vaginal applicator nightly for two weeks, then every other night for two weeks (8 per cent failure). All patients received this therapy over the period of a menses; five of these had senile vaginitis.

In sixty-one cases of vaginitis, the cervix received no additional treatment. There was no attempt to classify the trichomonas as the possible etiologic agent. Hydrogen-ion concentration readings were taken with nitrazine paper and the Beckmann pH meter. Smears or hanging drop were used to classify the vaginitis. Cultures were taken when indicated to exclude the gonococcus, as no acute gonorrhea was included in this series.

Most of these patients were office cases, and the ages ranged from teen-age to menopause (senile vaginitis). There were added to this number (sixty-one cases), ten cases of monilia, six of which were pregnant. These were treated with self-application of buffered acid jelly alone with disappearance of the monilia in all 6 cases. Four other cases were treated with 10 per cent and 20 per cent sulfa jelly with the report of one failure. Treatment was as above (5 c.c. to 10 c.c. nightly for two weeks, then every other night for two weeks).

For the type III smear vaginitis, 20 per cent sulfa jelly (#151-3-B-4) restored a type I vaginal smear eight days quicker than when the 10 per cent sulfa jelly was used, and 14 days quicker than when the buffered acid jelly without sulfa drug pH 4.5 was used. However, buffered acid jelly alone was as effective in changing the type II smear vaginitis to type I as when the sulfa jelly was used with it. This was not the case in type III smear vaginitis which required the use of the sulfa drug. Trichomonas was most common and was seen in about 80 per cent of the persistent type II smear vaginitis. Trichomonas was not observed often in the pH 6.5 to 8.0 type II smear or hanging drop.

Thus it would seem that buffered acid jelly alone was effective in trichomonas vaginitis therapy. This observation seems to be confirmed by Allen and Baum who reported extensively on the vaginal use of buffered acid jellies, which gave symptomatic relief in 84 per cent of their cases.⁷

Discussion

There are presented here 112 cases of conization of the cervix and 71 of vaginitis. In our hands the addition of sulfa drugs to the pH factor has been as great an improvement as the pH factor was over older methods of antiseptics used 10 years ago in the management of cervicitis and vaginitis. Cervical stenosis is most notable by its absence since using sulfa drugs after conization. Mild bleeding is little if any reduced over the old beta-lactose technique. Secondary bleeding and hemorrhage is reduced, as infection is definitely less after conization. The speed of cervical healing with low morbidity is noteworthy. Three weeks for complete healing of the cervix after conization may be expected with the use of sulfa drugs in buffered acid media.

In view of the fact that buffered acid jelly containing 20 per cent sulfathiazole is experimental and not commercially available, we are also

using buffered acid jelly and vaginal sulfonamide suppositories but with less favorable results to date.

Conclusions

1. The bacteriostatic effect of sulfathiazole and sulfanilamide is demonstrated by local applications to cervix and vagina without appreciable absorption.

2. Controlling the vaginal pH to 4.0 to 4.5 by the addition of buffered acid jellies is of value in the management of cervicitis and vaginitis, especially the trichomonas type of vaginitis.

3. Combining the sulfa drugs and buffered acid vaginal jellies gives the most effective therapy in cervicitis (conization post-operative management) and vaginitis of all types.

4. Conizations of the infected cervix may be safely performed in cases of acute gonorrhea when positive cervical cultures have persisted after oral administration of sulfathiazole; providing sulfa drugs in acid media are used locally during the healing period and at the time of conization. Negative cultures will then be the rule.

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THE UTERINE CONTRACTION PATTERN OF FALSE LABOR AND ITS RELATION TO PREMATURE LABOR

A Study of 16 Patients With the Lóránd Tocograph

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ONE of the problems of false labor which bears investigation lies in distinguishing it from true labor. Beck¹ states that the false pains are irregular, that they differ from those of true labor, but lists no other distinguishing characteristics. Adair² considers the chief difference to lie in the fact that the contractions of false labor fail to advance the process of labor, and also that the contractions which occur during false labor do not increase progressively in either frequency or duration.

White³ distinguishes false from true labor according to the following criteria: (a) true pains are felt in the back while false ones are located in the abdomen; (b) true pains are regular in occurrence and are associated with a hardening of the uterus, whereas false ones occur irregularly and are not accompanied by hardening of the uterus, (c) if the internal os will admit a finger, the membranes will be felt to become tense only in the presence of true pains.

On the hypothesis that false labor might be distinguished from true labor on the basis of a significant difference in the contraction patterns, as revealed by the Lóránd tocograph, we examined the tocographic records of all of our patients who experienced painful uterine contractions during pregnancy. Information gained from this source forms the basis for the present report.

Materials and Methods

The uterine contractions which take place during pregnancy were studied in a series of 1,119 tracings secured from ward patients in the Hospital of the University of Pennsylvania between August 1, 1938, and January 1, 1943.

Records of patients in this group, who were experiencing pain in association with their contractions—and of such a degree as to result in a diagnosis of false labor—form the basis for the present report.

Results

Sixteen women supplied observations for consideration. Table I summarizes information upon: (a) the time in pregnancy at which the false labors were registered; (b) the weights of the infants at birth; and (c) the character of the contraction patterns.

The uterine contraction pattern of pregnancy can be distinguished usually from that of labor. The former, Fig. 1, may record no contractions, or waves of irregular size and shape, and ones which usually

are relatively aperiodic in occurrence. The labor pattern, Fig. 2, is composed of waves which resemble each other closely in magnitude and shape, and ones which are relatively periodic in occurrence.

Contraction Pattern of False Labor.—The contraction pattern of the patient experiencing false labor resembles that of either pregnancy or labor. The data upon the sixteen patients mentioned above are arranged in Table I according to that classification. Half of the women exhibited the pregnancy pattern, and the other half the labor pattern. The occurrence of both patterns in association with false labor suggests that the pattern is of little or no value in distinguishing between false and true labor.

The Time of Occurrence of False Labor.—Table I records: (a) the interval between the tracing of the false labor pattern and the expected date of delivery; (b) the interval between the tracing and the actual date of delivery; and (c) the weights of the infants at birth. The expected and actual dates of delivery rarely coincided, and were of little value in determining how long before term the false labors took place.

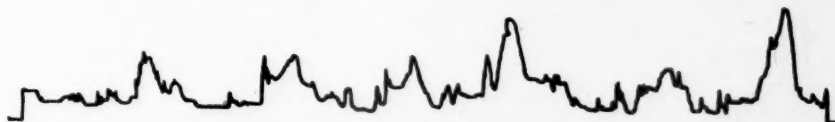


Fig. 1.—Normal pregnancy contraction pattern. Patient R. T. Tracing No. 165, made 11 days before labor. Note irregularity in size and shape of waves and their aperiodicity. The uterus of this patient was unusually active.

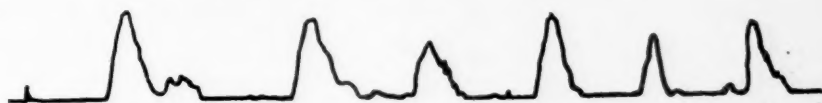


Fig. 2.—Normal labor contraction pattern. Same patient as Fig. 1. Tracing No. 179, made during first stage of labor. Note: A, disappearance of small waves, B, uniformity in shape of waves, C, magnitude of waves, and D, periodicity of waves.

TABLE I. PATIENTS EXPERIENCING FALSE LABOR

PATIENT		INTERVAL BETWEEN TRACING AND		INFANT BIRTH WEIGHT	TYPE OF CONTRACTION PATTERN
SERIAL NUMBER	TRACING NUMBER	DUE DATE	DELIVERY DATE		
		days	days	gm.	
1	232	8	8	3,654	Pregnancy
2	237	14	9	4,290	"
3	252	?	26	2,880	"
4	921	7	9	5,180	"
5	2,220	20	9	3,650	"
6	1,350	6	6	3,230	"
7	1,364	10	20	3,200	"
8	1,456	24	12	3,200	"
9	1,430	6	6	3,580	Labor
10	130	20	31	3,500	"
11	829	13	6	3,900	"
12	912	?	36	2,250	"
				2,640	
13	1,151	16	11	3,750	"
14	1,216	1	6	2,850	"
15	1,445	?	32	2,160	"
16	1,854	40	6	2,325	"

?: Due date in doubt.

Patient 15 experienced her false labor 32 days before she was delivered of a premature infant, i.e., weighing less than 2,500 grams. On the basis of the weight of her infant, therefore, she must have experienced her false labor considerably prior to 32 days before the date of her expected confinement.

Patient 16 was delivered of a premature infant 40 days before the expected date of her confinement. Thus it would appear that these two patients both experienced their false labors before any of the other patients in the series, patient No. 12 with twins being excepted.

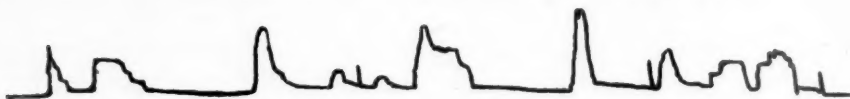


Fig. 3.—False labor showing pregnancy pattern. Patient J. A. Tracing No. 252, made 24 days before labor. Note irregularity in size and shape of waves and their aperiodicity. Compare with Fig. 1.



Fig. 4.—False labor showing labor pattern. Patient V. A. Tracing No. 1,445, made 32 days before labor. Note uniformity in size and shape of waves and their periodicity. Compare with Fig. 2.

Comment

The above observations would seem to justify the following comments: The uterine contraction pattern associated with false labor may resemble that of either pregnancy or true labor. This fact leads us to the conclusion that it cannot be employed as a means for distinguishing between false and true labor.

The untimely interruption of pregnancy is of such frequency and importance that every effort should be made to reduce its incidence. This is especially true in cases in which the patient has failed repeatedly to go to term. The present observations give rise to a thought which may aid in carrying some of these pregnancies to a normal ending.

The delivery of premature infants by patients 15 and 16, Table I, apparently followed false labors which occurred somewhat earlier than did those of patients who gave birth to full-term infants. Incidentally, although this observation may have no value, the contraction patterns of both patients resembled those of true labor. If these observations are true, they suggest that an early false labor may be followed by a premature labor. If such is the case, it would seem the part of wisdom to treat patients experiencing early false labors immediately, and perhaps at frequent intervals, with corpus luteum or other substances which have been recommended for the maintenance of pregnancy.

Summary and Conclusions

1. Tocographic records were made of the uterine contraction patterns of sixteen patients while they were experiencing false labor.

2. In some instances the contraction pattern of false labor simulated that of pregnancy, and in other cases resembled that of true labor. In view of this variability in the character of the contraction pattern associated with false labor, it is concluded that it does not offer a means for distinguishing between false and true labor.

3. Two patients experienced unusually early false labors, and gave birth to the only premature infants in the series. This association of the birth of premature infants with the occurrence of relatively early false labors suggests the advisability of treating patients who experience early false labors with corpus luteum or other substances recommended for the maintenance of pregnancy.

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PARASITIC OVARIAN CYSTS

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THE existence of ovarian cysts as parasitic tumors has been recorded by a number of observers. In 1860, Rokitsansky described alterations in the vascular supply which followed torsion of the pedicle of ovarian tumors. In 1892, August Martin published a report of two interesting cases of ovarian tumors with torsion. Spontaneous amputation of the pedicle with revascularization of the mass was found at operation.

Prior to this the condition had been noted at the autopsy table. Kayser states that Morgagni described parasitic ovarian tumors as early as 1748. However, today, they are rather unusual, undoubtedly because operation is performed earlier for symptoms suggesting torsion of an ovarian tumor.

The development of parasitic tumors may be divided arbitrarily into four stages depending on the degree of diminution of the primary blood supply. They are not completely separate phases but they represent, rather, a progression to the parasitic end result.

The *first stage* of reduction in the original vascular supply is due usually to a slow torsion of the mass on its pedicle. Infrequently with ovarian tumors, but more common with other pedunculated tumors, such as uterine fibroids, this may be due to growth of the tumor to the point where the blood supply through the pedicle becomes inadequate.

The etiology of pedicle torsion has been attributed to many causes and is probably a combination of several. Growth of the mass with traction and elongation of the pedicle certainly is a predisposing factor. Sellheim¹¹ believes torsion is secondary to external stress with resultant alteration of intra-abdominal tension. Others would prefer to relate it to intestinal peristalsis, corporeal movement or congenital variations. Bass¹ points out that pregnancy, with its resultant pelvic displacements, may play an important role in some cases.

In the *second stage* adhesions between the mass and adjacent tissues or the omentum are formed. These may be stimulated by the appearance of localized areas of aseptic necrosis at the periphery of the mass, most distal to the blood supply. Geist³ has pointed out that regressive changes in the ovary are common manifestations of decreased vascularity. Thus, edema, hyaline scarring, calcification and even bone formation may be found.

The *third stage* occurs with additional torsion and the further decrease in the primary blood supply. Secondary vascularization through the adhesions follows. In this phase, the tumor becomes semiparasitic receiving its blood supply from two sources: its pedicle, and the newly formed collaterals from the vessels to the adjacent tissues.

The *fourth stage* is represented by additional torsion to the point of complete amputation of the pedicle. The tumor now takes on a completely parasitic existence. The pedicle tends to become atrophied and fibrotic. At operation it no longer may be recognized as such, and the mass, for excision, must be separated solely from the adjacent tissues.

The entire process must be a slow one to permit new vascularization prior to complete loss of the original. The various stages which follow progressive torsions probably are represented in the symptomatology presented by the patient as recurrent attacks of abdominal pain.

Among the ovarian parasitic tumors, the type most frequently seen is the dermoid. This is as would be expected, since the ovarian dermoid often is subject to torsion. Serous cysts, solid ovarian tumors and relatively normal adnexa have been reported.

The organ with which these parasitic cysts are most often associated is the omentum, where they tend to become embedded. However, they have been found attached to the uterus, the broad ligament, the bowel and the bladder. The parietal peritoneum is involved occasionally.

Most of the parasitic ovarian tumors which have been described have not been very large. However, it is possible for them to continue to increase in size after the new source of blood supply has been established. Truesdale¹² reported the removal of a parasitic cystadenoma of the ovary weighing ninety pounds. He quotes Smith as having presented a case before the Massachusetts Medical Society where the tumor weighed 192 pounds, and the primary pedicle measured no more than one-half inch in diameter.

An accurate preoperative diagnosis of parasitic cyst of the ovary has not been made. A history of repeated attacks of lower abdominal pain associated with the findings suggestive of an ovarian mass in an abnormal location may indicate its presence. Pain has been the predominant symptom in almost all of the recorded cases.

Case Report

B. H., aged thirty years, was admitted to the hospital on January 5, 1943, the first admission of a gravida 2, para 2 complaining of attacks of pain localized to the right lower quadrant. These have recurred frequently during the previous six months, but seemed to have no relation to her menses. There had been no nausea or vomiting. The menstrual periods were regular, but during the last three periods the patient had noted some hypomenorrhea. No dysmenorrhea had been present.

The patient recalled somewhat similar attacks about five years prior to the present complaints, but stated that they had subsided spontaneously. She was entirely free of pain during the interim.

Her past medical and obstetric history was irrelevant to the present condition.

Physical examination was normal except for the pelvic findings. In front of the uterus a rounded, movable, nontender mass, the size of a peach, was palpated. Posteriorly and somewhat to the right another mass, the size of an orange, could be distinguished. A third mass, the size of a walnut, was palpated laterally and to the right. The uterus could not be satisfactorily outlined. Impression at that time was probably multiple cysts of the ovaries, perhaps dermoid in origin. The possibility of pedunculated fibroids was also considered.

Laboratory Data.—Blood and urine studies were all within normal limits. Scout film of the abdomen and intravenous pyelogram were reported as follows:

"Both kidneys are normal in all respects. There are several clusters of calcification within the pelvis, one having the typical appearance of a calcified fibroid. Below this fibroid is another circular calcification which may be an additional fibroid.

"Intravenous pyelogram reveals no abnormality in either urinary tracts or urinary bladder. The calcified fibroids cause extrinsic pressure on the urinary bladder."

Operation.—Exploratory pelvic laparotomy was performed on January 9, 1943. The right ovary was found to be converted into a multilocular dermoid cyst containing three separate portions. It was attached laterally by the right infundibulopelvic ligament about which the amputated right tube was twisted. It was attached also to the peritoneum over the dome of the bladder by a pedicle. Both of these pedicles were twisted; the infundibulopelvic three complete turns, the peritoneal not accurately determined. A single smaller dermoid cyst, probably part of the right ovary, was found embedded extraperitoneally in the right lateral pelvic wall.

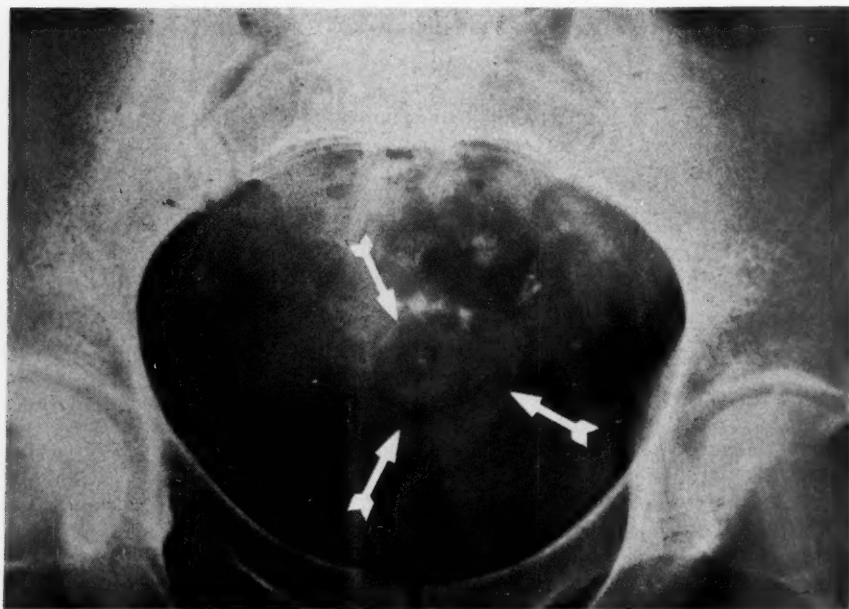


Fig. 1.—X-ray of the Pelvis. Arrows show circular area of calcification.

The uterus was normal in size and an amputated stump of tube about 2 cm. in length was noted coming from the left horn. Posterior to the uterus another cyst was found which, when delivered, was attached completely to the omentum by a pedicle. This was twisted $2\frac{1}{2}$ times on itself, but a new band from the omentum to the lateral aspect of this cyst was not twisted. This tissue was the size of a lead pencil and contained blood vessels, additional vascular supply to the tumor (see Fig. 2 for relationships of these cysts). The left infundibulopelvic ligament was not found.

The three cysts were removed and, after adequate peritonization of the pedicle stumps, the abdomen was closed without drainage.

Postoperative Course.—The patient made an uneventful recovery and left the hospital on the thirteenth postoperative day. When seen in follow-up clinic two months later, she was quite well, except for beginning menopausal symptoms for which estrogen therapy will be given.

Pathology.—Study of the tumors revealed the right ovary to contain two attached dermoids. It also showed marked edema, follicular cysts and a hemorrhagic corpus luteum. The parasitic cyst found in the omentum was a necrotic and calcified dermoid. However, within its wall, ovarian tissue definitely could be recognized. The third mass, the one found extraperitoneally, was also a necrotic and calcified dermoid.

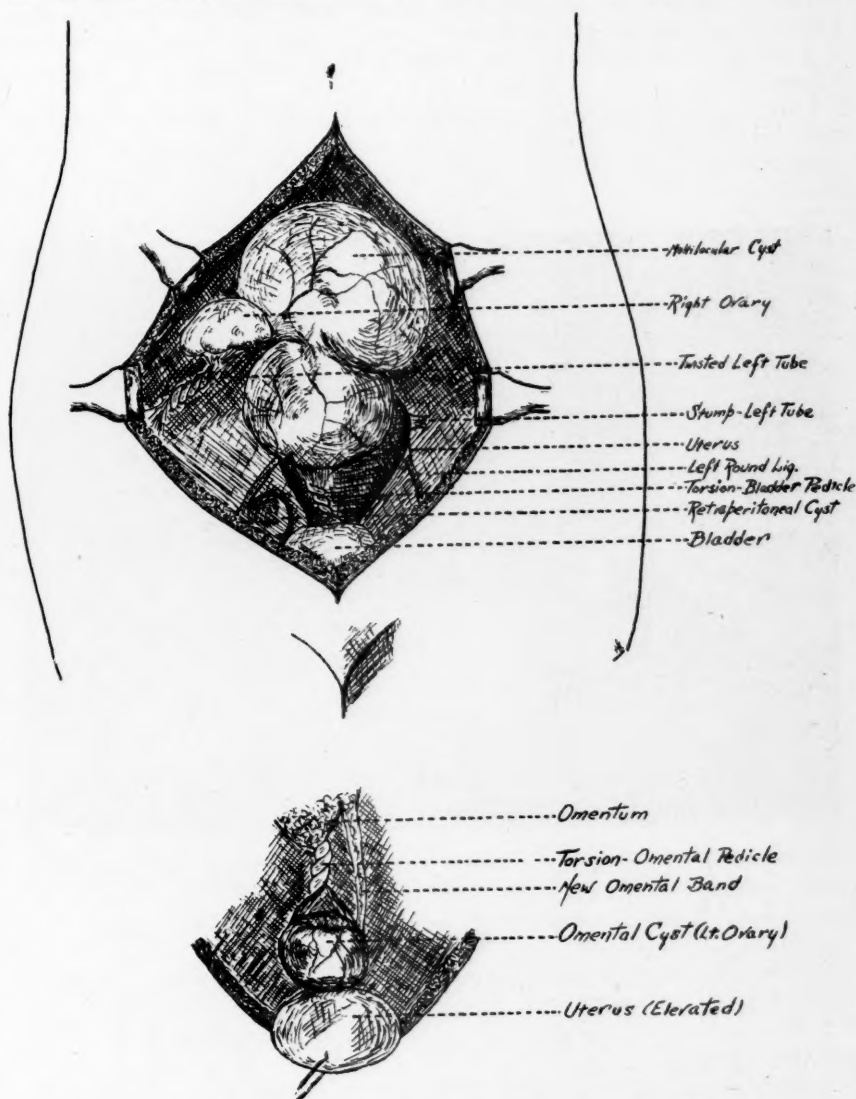


Fig. 2.—Relationship of the cysts as found at operation.

Comment

Reconstruction of the pathogenesis in the development of parasitic tumors could be done by careful examination of these cysts and their relationships. The later stages described above can be recognized in the drawing of the pelvic viscera as noted at operation. The main

portion of the right ovary was semiparasitic, the left completely so. The torsion of the omental cyst represented a beginning decrease of the secondary vascular supply. The new band of tissue suggested the beginning of the tertiary. The calcified and necrotic dermoid found in the lateral pelvic wall probably indicates the end stage of this development, a quiescent, completely parasitic, degenerated tumor. The patient's complaints of pain were amply explained by the pathology found. Because we are alert to the surgical emergency of torsion, the end result of progressive slow torsion, as represented by this case, is seldom seen.

This report incidentally may shed light on some of the unexplained omental dermoids. Almost all of the reported cases have occurred in women. We were able to establish beyond doubt the ovarian etiology in this case.

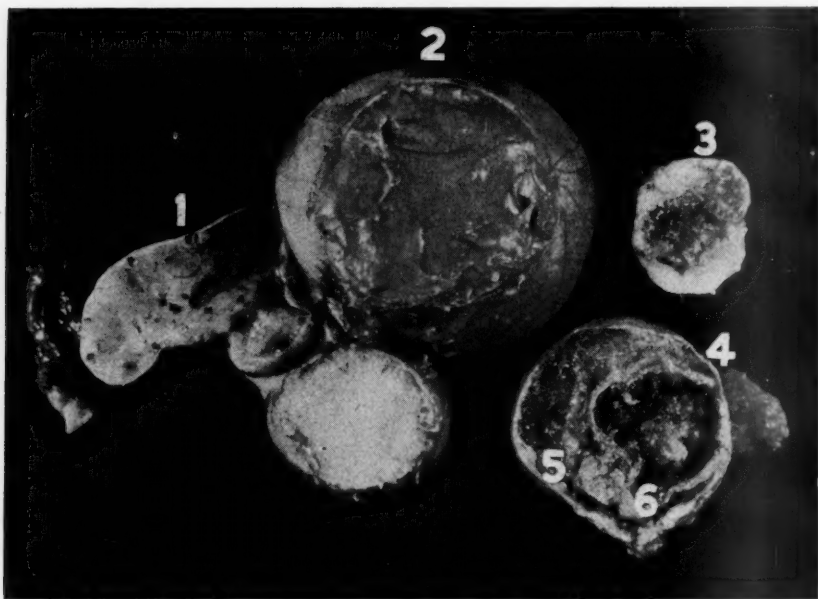


Fig. 3.—Showing 1. Right Ovary. 2. Multilocular Cyst. 3. Retroperitoneal Cyst. 4. Omental Cyst. 5. Ovarian Tissue. 6. Dermoid.

Summary

1. The literature on parasitic ovarian cysts has been briefly reviewed. Pathogenesis with arbitrary division into four stages is discussed.
2. A case with three parasitic dermoid cysts involving both ovaries has been presented.
3. The finding of ovarian tissue in the omental cyst may explain the etiology of some dermoid cysts thought to be primary in the omentum.
4. The evidence of calcification found by x-ray and histological study are indicative of the degenerative changes associated with slow pedicle torsion.
5. The case also demonstrates the process of new vascularization following pedicle torsion.

I should like to express my gratitude to Dr. S. H. Geist, and to Dr. L. Strauss for their assistance in the preparation of this report.

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CAUDAL ANESTHESIA IN ONE HUNDRED SIXTY OBSTETRIC CASES

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WE REPORT herewith a series of one hundred and sixty maternity cases delivered in the White Memorial Obstetrical Hospital in which caudal anesthesia was employed during the course of labor. A few of these cases received the anesthetic just prior to delivery, but the majority were carried for periods ranging from 2 to 28½ hours.

Of the one hundred and sixty cases in which caudal anesthesia was attempted, one hundred and twenty-nine achieved a satisfactory degree of analgesia for labor and delivery, with the exception of thirteen cases in which supplementary agents were used to finish the repair, or during forceps delivery. In twenty cases the anesthesia was judged to be partial or in some manner unsatisfactory. Most of these were due to the needle slipping out and failure in replacement, though a few patients in whom the solution had been correctly placed had moderate residual pain in the fundus with the contractions, but sufficient perineal anesthesia for delivery and repair. The eleven failures were all judged to be due to inability of the operators to enter the canal.

More than one injection through an indwelling needle was given to one hundred and eight cases; these, therefore, are classified as continuous caudal block.

The second stage of labor is prolonged due to lack of expulsive effort of the abdominal muscles stimulated by pressure on the rectum as the presenting part descends. Operative deliveries have a higher incidence in this group than in those having other types of analgesia.

Deliveries other than spontaneous without episiotomy are tabulated:

1. Episiotomy and midforceps delivery	1, a primipara
2. Episiotomy and low forceps delivery	34, 7 multipara
3. Episiotomy and spontaneous delivery	20
4. Scanzoni maneuver and episiotomy	3, all primipara
5. Kielland rotation and extraction	2
6. Manual rotation and forceps	9, one secundipara
7. Deep transverse arrest and Kielland	1, primipara
8. Manual removal of placenta for which supplementary ether was used	1
9. Cesarean section, in which subcutaneous infiltration was also used	2

Discussion of Results

In the White Memorial Obstetrical Hospital during the period covered by this series of cases (January 1 to April 27) there were 581 deliveries of which 160 or 27.5 per cent received caudal injections. The incidence of operative delivery (not including episiotomy alone) for the entire 581 cases was 19.6 per cent, while for the patients receiving caudal anesthesia the operative incidence was 36.2 per cent. From January 1, to April 27, of 1942, there were 385 deliveries with an incidence of surgical interference of 15.6 per cent. This increased incidence of operative delivery was made up largely of outlet forceps and episiotomy which in this teaching hospital has not become a routine procedure. In hospitals where most primipara are delivered by this method the operative deliveries would not be increased to any great extent.

Failure of the head to rotate necessitated operative aid in fifteen cases or 9.4 per cent. Taken month by month, the incidence of manual aid for failure to rotate has varied from 1 per cent to 4 per cent for the entire number of deliveries. This clear-cut increase in occiput posteriors is probably due to the lack of "bearing down sensation" and accompanying expulsive effort which added to the uterine contraction secures more forcible descent and subsequent rotation. Another factor is the relaxation of levator ani and perineal muscles depriving the head of the "perineal scoop" which normally insures anterior rotation of the occiput. Manual and forceps rotation is accomplished with ease in the usual case under caudal anesthesia; the muscles of the pelvis are well relaxed, facilitating the procedure, and supplementary anesthesia is seldom necessary.

Quantitative estimation of blood loss with caudal anesthesia has not been made, but the distinct impression is gained by all members of the staff observing these cases that the blood loss is less than average. Many women are delivered with but a few cubic centimeters of blood mixed with amniotic fluid following the placenta.

Observation of cases following delivery aided by caudal anesthesia reveals certain complications of varying degrees of severity. About

half of the patients complain of tenderness on pressure over the sacrum which they seldom note before palpation by the investigator. Tenderness over the sacrum occurs chiefly in cases where entry of the canal was difficult, necessitating a number of "exploratory probings" with the needle, and is probably due to this trauma plus the irritating effect of the anesthetic agent.

We have studied the report of Block and Rochberg⁶ in the use of continuous drip caudal anesthesia for obstetrics. Our experience would indicate that a certain volume must be injected in a short time to achieve sufficient height of anesthesia. Quantities less than 15 to 20 c.c. fail to ascend high enough to obliterate all pain.

Like the foregoing authors we have had one case of respiratory failure. She had been given a first injection of 30 c.c. with anesthetic level five centimeters above the navel followed by two hours of anesthesia. When her contractions again became painful, a second injection of 30 c.c. was made in fractional 10 c.c. doses with a short interval between, this precaution being taken because of the relatively high skin level of anesthesia. Within a few minutes of the last injection she complained of dizziness, faintness, and tinnitus, and became unconscious. The extern watching the patient gave artificial respiration and summoned aid which was immediately available. Blood pressure and pulse were unaltered and the patient did not become cyanotic. She was placed on the delivery table and delivered with forceps, the cervix having dilated from three centimeters to complete in the two-hour interval. It was her third child. Shortly after the delivery was completed, artificial aid to breathing became no longer necessary, having been maintained for an hour. Infant and mother were discharged from the hospital on the tenth day with no apparent ill effects. This accident was probably due to anesthesia involving upper cervical motor roots.

Occasional cases show moderate drop in blood pressure after the first administration which levels off and approaches normal. The systolic seldom goes below 80 mm. of Hg.

A few patients have complained of pains in the posterior aspect of the thighs relieved by analgesics other than opiates. We have questioned the possibility of peripheral nerve damage as the result of prolonged bathing of the nerve trunks with anesthetic agents and we are studying certain of our cases with the chronaximeter. Animal experiments are under way, using varying strengths of solutions of anesthetic agents to determine effects of prolonged action on peripheral nerves. Results of these investigations will be reported at a later date.

One primipara has imperfect bladder sphincter control. She is improving under treatment. She was delivered by Scanzoni maneuver which might well account for the difficulty.

The mental reaction of the patient toward the procedure is favorable in most cases. The usual comment is that if another baby is ever expected they will ask for caudal anesthesia. A few dislike the needle and the necessity for remaining relatively quiet.

Malleable steel needles were tried, but they seemed to offer but little advantage over the conventional steel spinal needle. Our only breakage occurred in a patient who was allowed to move about at will and on whom we used a malleable steel needle. It broke after ten hours of anesthesia but was easily recovered by pressing the skin down over the retained fragment, allowing it to come through the original perforation, and it was withdrawn with a forceps. The patient did not know of the accident.

Caudal anesthesia was used in single injection in two cesarean sections. One was a severe diabetic, and the other had an upper respiratory infection and cervical dystocia. Local skin infiltration was used in both. Peritoneal anesthesia was complete from the caudal block.

We have had no instances of fetal death or even mild degrees of asphyxia. In two instances of occiput posterior, the heart tones became irregular, but after manual rotation and forceps delivery, the infants cried immediately and lustily. This favorable result with the babies recommends the method for the premature infant.

Both metycaine, 1½ per cent in saline, and procaine, 2 per cent, were used in this series, the former constituting the majority of the cases. We are not prepared to express an opinion as to their relative merits at this time.

Summary and Conclusions

1. Certain complications are discussed, including possible peripheral nerve damage, pain in lower extremity, tenderness over sacrum, and respiratory failure.

2. There is an increase in the incidence of operative deliveries, including manual and forceps rotation for occiput posterior positions. The incidence of the latter was more than twice that of the same of previous months.

3. The procedure should be adopted with due regard for the above factors, realizing that it is no substitute for good obstetrical management.

4. For these and other reasons we suggest that adoption of the procedure by hospital staffs be preceded by intelligent planning and liaison between members of obstetric and anesthesia sections.

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THE USE OF ENDOCERVICAL AND ENDOMETRIAL SMEARS IN THE DIAGNOSIS OF CANCER AND OF OTHER CONDITIONS OF THE UTERUS

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A STUDY of the diagnostic value of vaginal smears in carcinomas of the cervix and of the fundus of the uterus has been conducted for over three years in this institution. The results of this investigation, of which a preliminary account¹ has already been presented, will be fully described in a monograph.²

The diagnosis of cancer of the uterus by vaginal smears is based on the fact that, like all the epithelial tissues of the body, the superficial cell layers of the tumor are subject to continual exfoliation. The exfoliated cells mix with the secretions of the uterus and cervix, find their way into the vagina and may be recognized in a smear of vaginal fluid.

The rate of exfoliation is variable.² Certain types of uterine cancer, like adenoma malignum, do not shed as well as others. The number of exfoliated cells depends upon the type and the developmental stage of the tumor as well as upon the existence and extent of a blood discharge. It is therefore evident that in a smear prepared from fluid obtained directly from the endocervix or from the uterine cavity, the chances of finding exfoliated cancer cells would be much greater than in corresponding smears prepared from the vaginal fluid. Of course, the vaginal smear has the advantage of being easily prepared with fluid which can be obtained without inconvenience or danger to the patient. The procurement of fluid from the uterine cavity is a more delicate procedure and one accompanied by somewhat greater technical difficulties.

The credit for demonstrating to us the practicability of the endocervical or endometrial smear belongs to Dr. George Bourgeois, of the Margaret Hague Maternity Hospital, and to Dr. William Cary, of the New York Hospital. Bourgeois used a curved metal intrauterine cannula with one terminal and several lateral apertures, as is frequently employed in tubal insufflation tests. Cary's technique, which we are now using, is described in another article in this issue. The cannula developed by Cary can be easily introduced into the endocervical canal and the uterine cavity without causing trauma or appreciable discomfort or pain to the patient. From this standpoint, it should not be compared with any endometrial aspirating curette as used in obtaining endometrial biopsies where the element of trauma is always present. The fluid of the uterine cavity is obtained by mere suction and retains its normal cytology. The technique of fixing and staining the uterine smears is the same as that used for vaginal smears.^{2, 3}

Compared to the vaginal smear, the uterine smear shows a larger number and a greater variety of endometrial and cervical cells. As a consequence, the diagnosis of cancer of the cervix as well as of the

fundus, is greatly facilitated. The irregularities and abnormalities in the structure and size of the cells and of their nuclei are more apparent in the endometrial than in the vaginal smear. Anisocytosis, nuclear gigantism, atypical fragmentation of the nuclei, even mitotic figures are encountered more frequently.

Another advantage of the endocervical or endometrial smear is that it makes possible the procurement of uterine cells, even in the absence of bleeding. In the vaginal smear, endometrial cells are usually present when there is uterine bleeding, which carries the cells into the vagina. Therefore, in the normal cycle, endometrial cells are found in the vaginal smear chiefly during the menstrual flow, whereas with an endometrial smear one can obtain endometrial cells during all stages of the cycle as well as in amenorrhea and menopause.

On the other hand, the vaginal smear presents a distinct advantage because of its simplicity and the facility with which it can be applied as a general routine method. A vaginal smear can be prepared at any time and as frequently as desired, without discomfort to the patient, and the procedure can be entrusted to a nurse or even to the patient herself. From this standpoint, we believe that it will remain as a standard routine method, whereas the endometrial smear will be applied more selectively in cases in which additional information is desired, after considering all possible contraindications, more particularly those of infection or pregnancy.

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A METHOD OF OBTAINING ENDOMETRIAL SMEARS FOR STUDY OF THEIR CELLULAR CONTENT

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THE purpose of this contribution is to describe a technique for aspirating the endometrial and/or endocervical secretions for a study of their exfoliated epithelial content, as discussed in the accompanying paper by Papanicolaou and Marchetti, and to outline the steps by which the investigation was evolved. The apparatus somewhat resembles Randall's aspirating endometrial curette with which it should not be confused, for our procedure may be carried out repeatedly with little or no discomfort to the patient and without traumatism of the tissues.

In 1929,¹ the writer presented an analysis of 266 postcoital studies performed by a standardized technique with respect to patients' preparation, hour of study and aspiration of specimens. In that paper was illustrated a cannula* devised for this technique and it was so fashioned that one end made an airtight engagement with the tip of a standard

*Since this article was written, I learn that a cannula of similar type has been employed previously in examinations of the larynx.

Luer syringe while the other end was somewhat curved and graduated in caliber to fit the cervical canal snugly and thus small portions of mucus could be gently aspirated from any part of the canal below the internal os. This cannula was made of special glass and is familiar to many gynecologists.

This study was carried out as a routine gynecologic procedure to determine both quantitatively and qualitatively the reciprocal action of the wife's secretions and the husband's semen previously evaluated by direct study. Certain observations were recorded, the significance of which was not then appreciated. For instance, it was noted that in many patients the quantity and viscosity of the cervical secretion varied at different times in the menstrual cycle, and that this secretion was most favorable for sperm cell survival and migration a few days after the cessation of menstruation. As the ovarian follicular cycle and the time of ovulation were more and more elucidated by the work of numerous investigators, it was apparent that this most favorable period evidently coincided with the preovulatory or high follicular phase. At this stage in the normally fertile woman, the uterine secretion is usually found to be more abundant, invariably alkaline (pH 7.5 or higher), transparent, mildly viscid and easily aspirated.

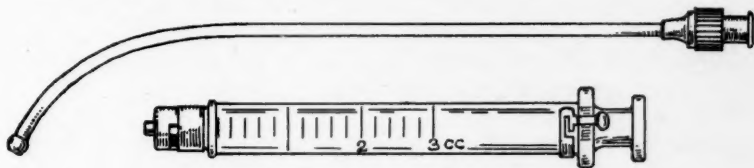


Fig. 1.—Intrauterine aspirating cannula.

The epithelial cells exfoliated from the uterine canal and almost invariably noted, singly and in groups, in smears prepared from uterine secretions were, however, wholly unappreciated as possible diagnostic criteria. It was after such smears were properly fixed and stained by the method developed for vaginal smears² that their potential diagnostic value was recognized by Papanicolaou to whom they were first submitted for a cytologic study.

In the meantime, a technique had been developed for securing fluid directly from the fundal cavity for study of the migration of spermatozoa in certain obscure cases of female infertility. Endocervical or endometrial smears and vaginal smears were prepared at specified times during the cycle, immediately fixed and submitted for investigation. Cases were selected which presented symptoms of functional deficiency and in which the likelihood of interrupting pregnancy was at a minimum.

Technique

The cannula used in securing these specimens is metal and similar in size to a uterine sound (6 F.). The overall length is 28 cm. (Fig. 1). At one end of the shaft is a broad flange within which is a thread enabling a firm union with a Luer syringe of 3 c.c. capacity, while the other, or uterine end, has a small bulbous tip. The malleability of the cannula makes it possible to shape it appropriately for introduction through any cervical canal not blocked by stenosis or extreme flexion. Endocervicitis is, of course, a contraindication to any invasion of the

uterine cavity. The cannula should be sterile and dry so that moisture in its channel will not distort the cells in the smear.

After a vaginal smear is obtained, the cervix is exposed with a speculum and any mucous wick extending from the external os is wiped away, as this is contaminated with bacteria and other vaginal elements. A simple antiseptic is applied to the surface of the cervix and the cannula introduced in the same manner as a sound. Even the discomfort of a tenaculum may be usually avoided. After introduction, the plunger of the attached syringe is withdrawn a short distance until resistance is felt and then the cannula is removed without further suction and a minimum or more of mucus can then be expelled upon a slide. This is thinly distributed and immediately fixed in alcohol and ether. The microscopic findings are reported in a separate article by Papanicolaou and Marchetti in this issue.

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57 WEST 57TH STREET

THE USE OF A PRECOITAL DOUCHE IN CASES OF INFERTILITY OF LONG DURATION*

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DURING the past fourteen months, we have observed an extended trial of a precoital douche in cases of long-standing infertility where no obvious reason for the failure to conceive was apparent. We believe that the number of conceptions presumably resulting from the use of this technique justifies a preliminary report in order that further data can be collected by a more widespread use of the method.

The use of the douche to be described was suggested as a result of studies over a period of years at Cornell Medical College on the metabolic behavior of human spermatozoa.^{1, 2} In these experiments, the spermatozoa are removed from the seminal fluid by centrifugation and transferred to a balanced salt solution containing glucose. It was found that maximal motility was maintained for many hours at 38° C. in this medium as long as an adequate supply of glucose was present. In the absence of glucose, motility failed rapidly and further investigation showed that the only foodstuff used by human spermatozoa for the production of energy for motility was glucose or any other utilizable carbohydrate (fructose, mannose, maltose and glycogen can be substituted). Furthermore, when motility failed in the absence of glucose, it could be restored maximally by the addition of glucose. In view of

*Aided by a grant from the National Committee on Maternal Health.

these facts, it was considered possible that the use of Ringer-glucose solution as a precoital douche in certain cases of infertility would be preferable to less physiological media such as bicarbonate.^{3*}

The first suggestion that Ringer-glucose solution (9 grams NaCl, 0.23 gram KCl, 0.22 gram CaCl₂, 20 grams glucose (C.P.) to 1,000 c.c. distilled water) might have value arose from a case referred to one of us (R. S. H.). The history is as follows:

Case 1.—Married six years. Contraceptives used one year. Coitus practiced very irregularly because of dyspareunia. Operation in 1937 to enlarge vaginal opening and previous unsatisfactory entrance corrected. Intercourse thereafter averaged two or three times a month in midmenstrual period. Periods regular. Husband referred for semen examination January, 1942. Excellent semen specimen, vol. 4.5 c.c., count, c.c. 263 million, motility and morphology good. Husband disclosed that wife had always used a bicarbonate douche as a lubricant just prior to intercourse.

Treatment and Result.—Ringer-glucose solution (250 c.c. to 500 c.c.) prescribed as a precoital douche to replace the bicarbonate during the fertile period. Wife conceived in first month with only one "contact." Delivered spontaneously of normal, male child.

Our reaction to this result was to consider it a coincidence. However, a similar case was presented shortly thereafter and when conception occurred in this instance almost as rapidly as in Case 1 after use of the Ringer-glucose douche, we asked several gynecologists to give the technique further trial in selected cases. The histories and results are as follows:

Case 2.—Infertility of four years' duration. No obvious defect in wife. Tubes patent, menstrual history and repeated spermigration studies normal. Vaginal smears normal which indicated ovulation between eleventh and thirteenth day of cycle. Endometrial biopsy normal. Cervical os small, dilated two and one-half years ago. Husband's specimen good, vol. 3 c.c., count, c.c. 250 million, 94 per cent normal forms and good motility. Artificial insemination with husband's semen tried eight to ten times without success. Alkaline douche used for several months without success. Ringer-glucose douche advised and conception took place in second month of trial. Spontaneous delivery of healthy male child.

Case 3.—Infertility of 2 years' duration. No obvious defect in wife. Menstrual cycle 33 to 34 days. Husband's semen specimen normal, vol. 2 c.c., count, c.c. 110 million, normal morphology and good motility. Use of Ringer's glucose douche was advised just before intercourse on the eighteenth, twentieth and twenty-second days of cycle. In first month of trial, douche used for first time on the eighteenth day and again on the twenty-second. No other intercourse during that cycle. Conception took place in this month and gestation has followed a normal course until now. Unfortunately, for a more careful control in this case, the gynecologist in charge also tried one artificial insemination using the husband's specimen on the eighth day of the same cycle.

*We have recently seen a similar statement by Rubin.⁴ "Better than sodium bicarbonate or sodium phosphate douches are the physiologic isotonic solutions, Ringer's and Locke's solutions. These are, unfortunately, better founded on theory than upon actual therapeutic experiences." From this statement, we assume that no actual experiments with these solutions were tried.

However, since the cycle in question was one of 33 to 34 days, it is unlikely that ovulation took place on the eighth day though the possibility cannot be excluded.

Case 4.—Infertility of 4 years' duration. In 1939, insufflation revealed patent tubes and menstrual history normal, 28-day cycle. Husband's specimen good, vol. 1.9 c.e., count, c.e. 120 million, good motility and morphology. In 1939, artificial insemination with husband's specimen without success. In 1940, operation disclosed small fibroid myomas and small ovarian cyst which were removed. Endometrial biopsy essentially normal with only possibility of slight corpus luteum deficiency. In 1941, couple advised to use fertile period and corpus luteum given by injection 11 days before onset of period without success. Ringer-glucose douche suggested in March, 1943, and used on the thirteenth and fifteenth days of that month's cycle. Patient did not menstruate again and a positive pregnancy test was obtained April 26.

Case 5.—Infertility of 2½ years' duration. Gynecological examination normal in every respect. Husband's specimen good, vol. 6.5 c.e., count, c.e. 70 million with good motility and morphology. Ringer-glucose douche advised September, 1942, and conception took place January, 1943. No other therapy given.

Case 6.—Infertility of 14 months' duration. Gynecological examination normal in every respect. Husband's semen specimen rather poor, vol. 4.2 c.e., count, c.e. 17 million. Wife on thyroid therapy since July, 1942. Ringer-glucose douche advised in September, 1942, and conception took place following month.

Case 7.—Infertility of 6 years' duration. Normal gynecological examination except for thick endocervical secretion. Postcoital spermigration test negative. After Ringer-glucose douche, 30 to 40 active spermatozoa crossing h. p. f. in cervical mucus. Husband's specimen only fair, vol. 3 c.e., count, c.e. 50 million, motility good but 22 per cent abnormal forms. Advised Ringer-glucose douche and conception took place in second month of trial. Spontaneous delivery of healthy female child followed in due course.

Case 8.—Infertility of five years' duration. Twenty-six- to 29-day cycle. Severe dysmenorrhea with leucorrheal discharge for one week prior to menses. Had previous history of "injections," D and C, insufflation test and artificial insemination (husband's specimen). Latest gynecologic-abdomino-pelvic examination negative but for acutely ante-flexed uterus with cervix in axis with vagina. Repeated spermigration tests negative. Husband's semen specimen, vol. 5 c.e., count, c.e. 37 million, 35 per cent abnormal forms. No report on motility.

Treatment.—Cervical dilations monthly either on ninth, tenth or twelfth day with coitus following Ringer-glucose douche. Conception in the third month of therapy. Abortion at fourth month of gestation.

Case 9.—Infertility of 2 years' duration. Menses normal. Twenty-eight to thirty day cycle. Previous treatment for erosion of cervix. Gynecologic-abdominal-pelvic examination negative. Tubal insufflation and hysterosalpingography were normal. Repeated spermigration tests at resumed ovulation period showed no sperm in cervix. Endo-

metrial biopsy showed progestational endometrium. Husband's semen good, vol. 5 c.c., count, c.c. 163 million with normal motility and morphology.

Treatment.—Repeated cervical dilations monthly either on tenth, eleventh or twelfth days for fifteen months. Coitus during fertile period without success. Advised Ringer-glucose douche during fertile period and conception occurred in first month of trial. Delivered spontaneously of healthy male child.

Case 10.—Married nine years. Conceived and delivered spontaneously in first year of marriage. Four years of contraception followed. No conception for four years after cessation of contraception. Gynecologic-abdomino-pelvic examination and tubal insufflation normal. Sperm-migration tests negative during probable fertile period. Husband's semen good, vol. 3 c.c. count, c.c. 90 million, good motility and 18 per cent abnormal forms. Ringer-glucose douche advised and conception took place in second month of use. Healthy female child delivered.

Case 11.—Infertility of 14 months' duration. Irregular menses; 33 to 53 day cycle. Tubal insufflation showed patent tubes. Sperm-migration test revealed motile spermatozoa in cervix. Husband's semen reported as good but no details given. Ringer-glucose douche advised and it was used indiscriminately during first month of trial. No menstruation followed and patient is now in sixth month of gestation.

Case 12.—Case of artificial insemination with use of donor semen. Patient inseminated for five consecutive months on days 8 and 12, 11 and 15, 12 and 14, 10 and 14, and 9 and 13, without success. The following month, a Ringer's glucose vaginal douche was given just prior to insemination on days 12 and 14. Fertilization occurred in this month. Patient is now in seventh month of gestation.

Discussion

It might well be argued that these cases are coincidences or that other and simultaneous therapy confuses interpretation of the results. In view of the fact that many conceptions take place without therapy even after many years of infertility, it is within the bounds of possibility that several of the cases reported here would have conceived eventually. However, we believe that it is more than coincidence that, in twelve cases averaging 3.3 years of infertility, conception should take place on the average within two months (and not more than four months) after use of the douche and after all other therapy had failed. To our knowledge, the number of cases in which the douche has been used is not more than sixty. In many of these instances, the douche was begun only within the past three months so that more complete results are not available. We present these results with caution and with the emphasis that the efficacy of the technique may be restricted to the type of infertility in which both partners show no striking abnormality. On the other hand, we call attention to cases 6, 7 and 8 in which the semen specimens which produced conception were rather poor.

Lastly, in analyzing the reason for the successes listed above, it is possible that such a douche removes temporarily some incompatibility

which prevents the migration of the spermatozoa through the cervical canal. Certainly, if any douche is to be used at all, it would be advisable to use one in which the spermatozoa are known to maintain full motile activity for many hours. We added glucose to the balanced salt solution for the reason already given, namely, that glucose is the primary foodstuff from which the spermatozoa derive the energy for motility. However, it should be noted that in normal circumstances, the seminal fluid contains an abundance of this essential substance and that there should be little need for a further supply. The possible importance of a seminal pool around the external os aiding in the migration of the spermatozoa from the vagina into the cervix cannot be lightly dismissed. In this sense, any increase in the volume of this pool would be of benefit and, in view of known facts, no better diluter could be found than Ringer-glucose solution.

We are deeply indebted to Drs. S. Siegler, C. McLane, A. Greeley, H. Whiting and A. Stone (all of New York) for case histories 3 to 10.

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SKELETONIZED FETAL REMAINS

Report of Two Cases With Unusual Termination of Pregnancy

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SKELETONIZED fetal remains constitute a rare and most interesting condition. The literature on this subject is large. Much of it, however, consists of single case reports and each of these, as a rule, represents a variation of its own. Recently we have encountered two cases so remarkable in their clinical and pathologic manifestations that we have considered them worthy of report.

CASE 1.—(HIST. NO. 208208. GYN. PATH. NO. 53034.) This 22-year-old colored female was admitted to the gynecological service of the Johns Hopkins Hospital on July 28, 1941, with the complaint of lower abdominal pains. The family history was noncontributory, and the obstetrical record was the only pertinent finding in the past history. She had had three pregnancies. The first and second were four and two years prior to admission. On May 12, 1941, she was delivered at home of a premature stillborn infant. The expected date of confinement for this pregnancy was July 15, 1941. Following this delivery she had normal menstrual periods—June 8 to 15, 1941, and July 14 to 18, 1941.

Ever since the delivery of this seven months' premature stillborn infant, two and a half months before admission, she had had persistent sharp pains in the right lower quadrant of the abdomen, which gradually became worse. Two weeks before admission she had profuse leucorrhea which abated with hot douches. There was slight nausea, but no vomiting. She believed that she had lost about 15 pounds.

On admission she was a well developed negress who was not in acute distress. Temperature 100°; pulse 98; respiration 22; and blood pressure 112/70. The general physical examination was negative. The abdomen was flat and relaxed. There was an irregular mass felt abdominally which rose to 3 to 4 fingerbreadths above the symphysis pubis. The vaginal outlet was a little relaxed and there was slight leucorrhea. There was a moderate erosion about the cervical os. Projecting from the right border of the uterus, and intimately associated with it, was a firm nodule about 8 cm. in diameter. The adnexa were normal to palpation. The laboratory findings showed a negative serologic test for syphilis, hemoglobin 10.5 Gm., white blood count of 8,450, and urine negative.

On July 29, 1941, a total abdominal hysterectomy was done by one of us (C. P. M.). Upon opening the abdomen it was found to contain about 300 c.c. of amber, clear fluid. There was a nodule arising from the right upper portion of the uterus, which made the total uterine mass about three times its normal size. Crepitation was felt in this mass. A ball of matted loops of intestines was adherent to this mass. The adnexal organs were normal.

The uterus measures 13 by 8 by 5 cm. The surface is smooth except over the apical portion, where there is a rough, slightly raised hemorrhagic and fibrous area which measures 4 by 4 cm. There is a definite asymmetry of the uterus, a nodule arising from the right cornual area to a much higher level than the left. This nodular mass measures 7.5 by 7 by 7 cm. and the roughening noted above is over the upper surface of this mass. Upon opening the mass the myometrium is 2 to 3 cm. thick and completely surrounds a definite cavity which is 4 cm. wide. This cavity is packed with fragmented and intact bony structures representing fetal skull bones, ribs, and long bones (Fig. 1). A femur can be identified and it measures 3.7 cm. in length. Many of the bones are firmly imbedded in the myometrium which surrounds the cavity. This lining myometrium has an orange-yellow discoloration, and this material seems to infiltrate, in streaks, the adjacent myometrial wall for most of its thickness. Between this cavity and the endometrial cavity the myometrium shows less of this purulent infiltration but more scarring. At the superior border the purulent material infiltrates flush with the surface roughening. The tubal stump on the right is situated higher than the left. The mass with its thickened myometrium is about twice the size of the rest of the uterus. No gross connection between the encysted mass of bones and the uterine cavity can be made out. The cervix is 3 cm. long and measures 2.5 cm. at the external os. The area about the portio appears normal and the endocervix shows no lesion. The uterine cavity measures 7 cm. in length. The endometrium is smooth, hemorrhagic to a slight degree, and measures 2 mm. in thickness. A probe can be passed from the endometrial cavity out through the left tubal stump, but no entrance of the tube from the opposite cornual area can be found into the uterine cavity.

The section of the cervix reveals a moderate cervicitis. Sections of the uterus showing the endometrium reveal an endometrial stroma of a loose fibrous texture. There is a minimal infiltration of the stroma with small round cells, and this infiltration is almost entirely confined to the surface regions. Most of the glands are small, circular, and straight, although a few of them show early tortuosity. The glandular epithelium reveals no secretory activity. The sections of the myometrium from about the encysted fetal remnants are very interesting. The inner portions show very heavy infiltration with plasma cells, lymphocytes, and polymorphonuclears. Many large cells, suggesting decidual

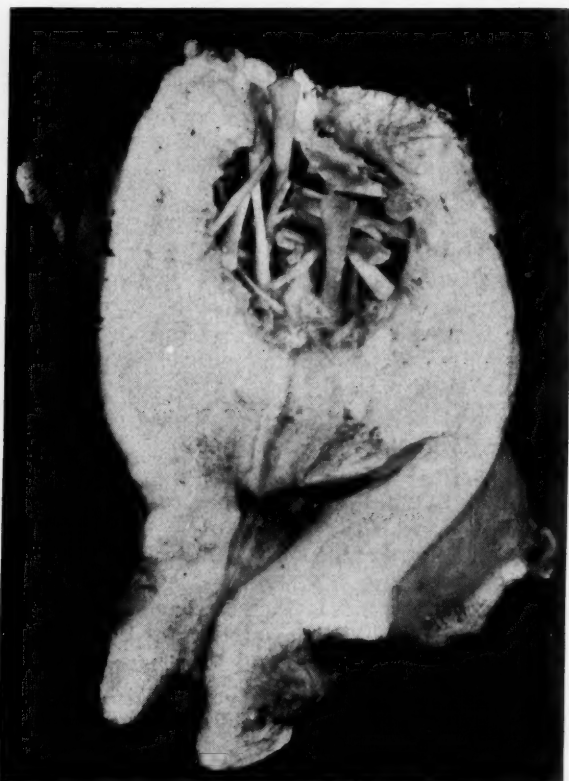


Fig. 1.—Case 1. The removed uterus with the intramyometrial encysted fetal remnants. Note the inflammatory reaction about the cavity and in the myometrium at the upper border particularly. Loops of intestines were adherent at the shaggy uterine surface above the mass.

cells, are seen and also a rare giant cell of the foreign body type can be seen, particularly about the engulfed bony fragments. As the periphery is approached, there are also large collections of inflammatory cells, mostly of the chronic type. These collections have a tendency to be arranged in linear streaks. The myometrium is much thickened and there is considerable scarring and disruption of the usual architecture. Most of the inflammatory reaction in the myometrium extends towards the serosal surface, but there is slight inflammation and scarring in the myometrium towards the uterine cavity. Near the surface and about the cavity the tissue is very vascular with extensive fibroblastic reaction. By consecutive sections the right tube can be followed

from the cornual stump interstitially to the very border of the encysted mass. The muscular tissue about the tube in its interstitial portion reveals the same subacute inflammation. The tubal mucosa is normal except for slight subacute inflammation. The lumen of the tube becomes larger as the bone-containing cavity is approached. Numerous sections were taken through the myometrium between this mass of bones and the endometrium, and no area is found which could be interpreted as tube or remnant of tube.

Pathology Report.—Cervicitis, chronic; endometrium, interval, non-secretory; myometritis, subacute; intramyometrial encysted fetal remnants.

Except for a mild and transient cystitis due to *E. coli*, the postoperative course was uneventful. She was discharged on the eighteenth postoperative day, and discharge examination revealed the vaginal vault to be well-suspended with very slight induration across the apex. Follow-up in one month and five months revealed the patient asymptomatic, the incision well healed, the vagina suspended adequately, and the pelvis free of induration and abnormal masses.

Discussion

A survey of the available literature has failed to reveal a similar case on record. The closest approximation is one of the cases reported by Smith² in 1933. He found a false intrauterine cavity containing a collapsed fetal skull in the uterus of a 29-year-old female who gave a history of leucorrhea and irregular bleeding following an induced abortion (at 4 to 4½ months), 11 years previously. This was the only known or suspected pregnancy. The picture of his gross specimen is in some respects identical with Fig. 1. Rubin² in a discussion of this case of Smith's cites a case of his in which he curetted two slender shanks of bone from a 25-year-old patient who complained of sterility and dysmenorrhea for seven years. When 18 years of age, she supposedly aborted a three months' fetus. The retention of fetal remnants and of suppurating fetuses in the uterine cavity because of missed abortions or missed deliveries is infrequent. Kelly and Cullen³ removed a uterus with a suppurating eight months' fetus one year after its delivery was expected, and in another case, four years after expected delivery.

It is difficult to interpret the findings in this case. It seems unlikely that these fetal remnants had been present for any considerable length of time, in view of the short duration of symptoms and the rather active inflammation about the bones. These bones may represent the remains of a true interstitial pregnancy occurring with the intrauterine pregnancy which later was delivered stillborn. The intrauterine pregnancy, as it developed to sufficient size, compressed and killed at twenty-two weeks the interstitial pregnancy. The soft parts of the interstitial pregnancy suppurated, leaving the cavity of fetal bones. The increase in diameter of the lumen of the interstitial portion of the right tube as it approaches the intramyometrial cavity suggests this possibility. Reports of simultaneous bilateral tubal pregnancies and of one intrauterine and one tubal pregnancy are frequent enough in the literature to suggest this explanation. The finding of decidua-like cells about the bones might mean that this pregnancy found a satisfactory nidus for implantation in an island of endometrium in this interstitial portion of the tube. Müllerian epithelial derivatives are known to be stimulated

to form decidual cells by pregnancy at any point in the tract without assuming that endometrial tissue was already present. Ash⁴ has given an excellent review of the subject of interstitial pregnancy up to 1932.

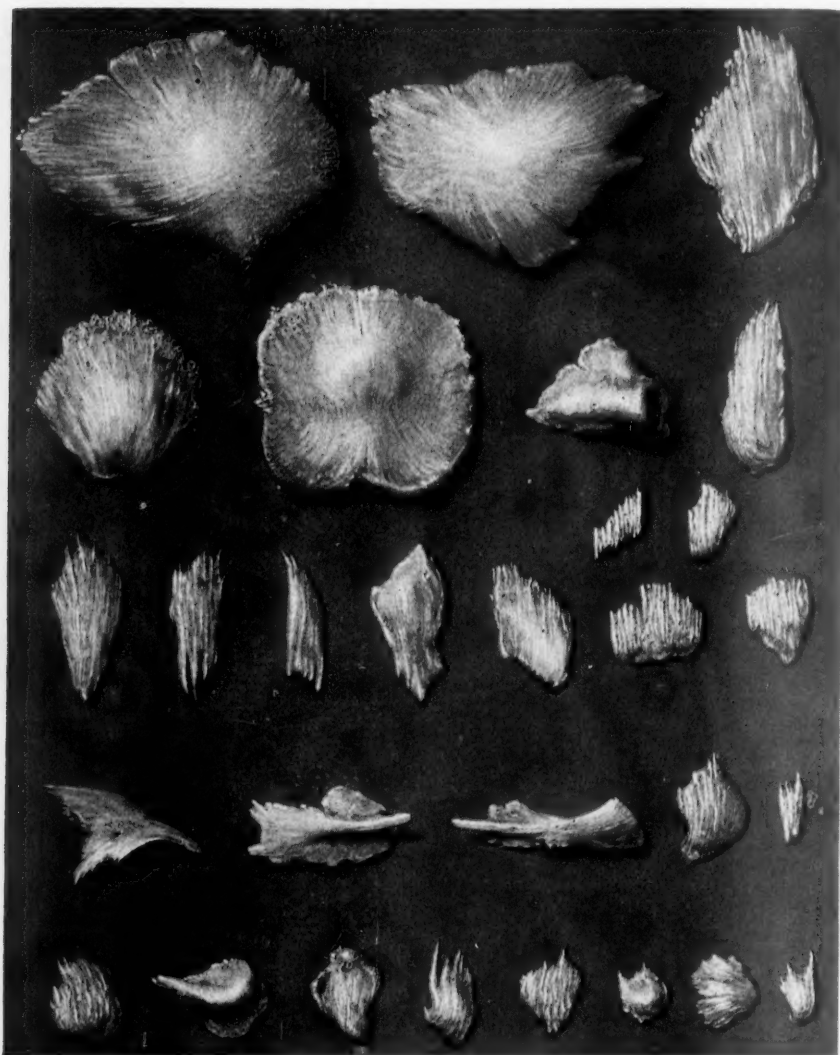


Fig. 2.—Case 2. The fragments of fetal skull bones eroding through and removed from vagina anterior to the cervix. Twice actual size.

CASE 2.—(HISTORY NO. 103324. GYN. PATH. NO. 51535 & 51639). This 21-year-old colored female was admitted to the gynecological service of the Johns Hopkins Hospital on December 1, 1940, with a complaint of left lower quadrant pain and dyspareunia. She was delivered of her first baby in 1937 by low forceps and episiotomy. Post partum she developed an ischiorectal abscess, which spontaneously opened into and drained through the vagina. No fistulous tract remained on discharge. A second fullterm delivery occurred in March,

1939, by elective low forceps and episiotomy. Since the birth of the first child a moderate leucorrhea had been present.

She was first seen in the Gynecology Dispensary on June 4, 1940. For two months she had pains in her lower abdomen and dyspareunia. Examination revealed a lacerated cervix, normal uterus, and bilateral adnexal thickening of slight degree. A diagnosis of chronic cervicitis and salpingitis was made and the patient was instructed to take douches. On July 2, 1940, she was again seen complaining of urinary frequency. The last menstrual period was May 21 to 25, 1940. A small urethral caruncle was found and the catheterized urine contained only two white blood cells per high power field. The fundus was uniformly enlarged to the size of a three months' pregnancy and the cervix was soft. She again reported on Nov. 5, 1940, with the story of an apparent miscarriage in August. During most of October she felt weak and had right flank pains radiating to the right lower quadrant of the abdomen. She did not menstruate in September, but had a profuse two weeks' period during the middle of October. On pelvic examination beneath the vaginal mucosa, anterior to the cervix, was a large piece of calcified material. The uterus was of normal size and fixed. In the left adnexal region was an adherent tender mass about 5 cm. in diameter and right adnexal region revealed thickening. Except for slight reddening about the trigone of the bladder nothing abnormal was seen through the cystoscope. A biopsy of the vaginal calcified material showed bone and chronic inflammatory tissue. She had a normal menstrual period November 14 to 17, 1940. On admission on Dec. 1, 1940, she was an asthenic Negress who did not appear acutely ill. Temperature 100.2° F.; pulse 96; respiration 24; blood pressure 130/75. The general physical examination was negative and the pelvic findings were as noted above. The impression was chronic salpingitis with tubo-ovarian inflammatory mass on the left, and possible vesical calculus eroding into the vagina. The laboratory findings showed negative serologic test for syphilis, hemoglobin 10 Gm., white blood count 11,600, urine negative microscopically, but culture revealed *E. coli*.

An instillation of methylene blue into the bladder with a sponge in the vagina showed no dye on the sponge after one-half hour. On December 5, 1940, the patient was taken to the operating room where 29 fragments of bone were removed by means of an incision in the vagina at the anterior fornix. Most of these fragments were very small, but a few of the larger fragments were identifiable as fetal skull bones (Fig. 2). The postoperative course was uneventful and the patient was sent home on the eleventh postoperative day. Laparotomy for removal of the tuboovarian mass from ruptured tubal pregnancy was not done because she was asymptomatic and because of the likelihood of spontaneous absorption. On follow-up in one year there was some induration in the anterior cul-de-sac about the vagina, but no calcified material could be felt. The uterus was normal, but a left adnexal mass extending into the posterior cul-de-sac could be felt, which was quite firm and very slightly tender. The patient was asymptomatic.

Discussion

Although it seems likely that fetal bones of a ruptured tubal pregnancy have eroded into the vagina before, we have been unable to find a report of such a case. Cullen⁵ has reported a case which was probably a secondary abdominal pregnancy following a rupture of a tubal

pregnancy that developed to eight months, and three years later a sac containing fetal bones was removed from the right lower abdomen. These bones had eroded into the bladder and into two areas of the cecum. Schewket⁶ had a case with an extrauterine fetus which 21 months later spontaneously discharged a necrotic tibia through the anterior abdominal wall. Gustafson, Meredith, and Hord⁷ reported a case in 1932 which discharged clavicle, ribs, long bones of extremities, and flat bones of the head through the rectum. There are several other reports of intestinal and bladder complications arising from the migration of fetal bones. A more frequent termination of ruptured (or unruptured) tubal pregnancy is the formation of a lithopedion. De Lee⁸ cites Wagner's case with a mummified fetus retained for 29 years, In Virchow's case the fetus retained for 28 years, and Smith reports fetus removed from a 94-year-old female 60 years after conception. Masson and Simon⁹ in 1928 reported 9 cases from the Mayo Clinic and collected 174 from the literature. In 1932 a case of an eight months' pregnancy calcified and retained for 40 years was noted by Titus and Eisaman.¹⁰ In 1935 Aschman and Helwig¹¹ reported two cases: one was a grapefruit-sized calcified mass removed from the left lower quadrant of a 69-year-old female 35 years after the last pregnancy. Hair, skull, legs and arms were identifiable. The other case was a mummified fetus weighing 546 Gm. removed from the right pelvic cavity of a 24-year-old patient fifteen months after conception.

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RHABDOMYOSARCOMA WITH ADENOCARCINOMA OF THE UTERUS

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THE occurrence of a rhabdomyosarcoma in the uterus, an organ which normally does not contain striated muscle, is extremely rare. Gunning and Ross¹ in 1940 were able to collect only ten such cases from the literature and added one of their own. The simultaneous occurrence of rhabdomyosarcoma with adenocarcinoma is even more unusual. However, the association of sarcoma with carcinoma of the uterus has been reported.²

Several theories have been expounded to explain the occurrence of rhabdomyosarcomas of the uterus. Pfannenstiehl in 1892³ believed them to originate in the connective tissue of the endometrium, which later undergoes metaplasia. This is not supported by fact, for the transformation of nonstriated muscle into striated muscle has not been demonstrated. However, Nehr Korn⁴ found fully differentiated striated muscle cells in two uteri removed after puerperal sepsis. Under pathologic irritation, these could well serve as the basis for the development of rhabdomyosarcomatous tumors. Wilms in 1899⁵ believed these tumors to originate in primitive mesodermal tissue which had been carried downward during the descent of the wolffian duct. Absence of striated muscle in the wolffian body together with the development of this tumor outside the course of the wolffian duct controverts this theory. In 1907 Mönckeberg⁶ suggested that these tumors arise from cell rests in the müllerian duct. The objection to this theory is the absence of mixed mesodermal tumors in the broad ligaments despite the migration of the müllerian ducts through them. Cohnheim⁷ suggested that among the differentiated cells of almost all tissues, there are rests of very immature indifferent or embryonal cells. These are available as sources for constant replacement, for regeneration after injury and for the proliferation of tumors. The very immature anlagen of smooth muscle cells can alter their usual course of differentiation and produce striated muscle tumors. The multiplicity of theories presented make it quite evident that the exact mode of origin of these tumors is as yet obscure.

There is much confusion in the literature concerning classification of uterine sarcomas, perhaps because of the rarity of these tumors. In 1892,³ Pfannenstiehl applied the name "Traubiges Sarkom" to a group of cases of sarcoma of the cervix and vagina which in the English literature have been called "botryoid sarcoma," in an attempt to describe their grapelike character. However, it must be pointed out that often they do not assume this gross appearance. In 1867, Weber⁸ introduced the concept of mesodermal mixed tumor of the uterus in the first case of its type described. Since that time Glass and Goldsmith⁹ were able to collect ninety-five cases of mixed mesodermal tumors of the uterus. However, many other types of sarcomas arising from the normal uterine constituents have been described. There may be very immature and indifferent types, the round cell, spindle cell or giant cell sarcomas, or less immature and better differentiated types, angiosarcoma, melanosarcoma, lymphosarcoma or leiomyosarcoma or mixtures of these in all possible combinations. Tumors composed of tissue which is foreign to the uterus may also occur. The case to be presented belongs to that group. It is one of rhabdomyosarcoma which, in addition, is associated with carcinoma.

Case Report

R. Z., 66-year-old German born, gravida 2, para 2, entered Mount Sinai Hospital on July 23, 1942, complaining of vaginal discharge of six months' duration associated with a 30 pound weight loss. Her past history was not pertinent to her present illness. Her present illness began six months prior to admission when she developed a vaginal discharge for which a "polyp" was removed by her physician. Symptoms persisted and another "polyp" was removed approximately ten weeks later. During this time the patient lost about 30 pounds and immediately prior to admission to the hospital, had begun to develop nausea and vomiting. Menopause had occurred seventeen years previously.

Physical examination revealed a well-developed and nourished female in no acute distress. Pelvic examination showed the cervix to be distended by a protruding necrotic mass. The uterus was irregularly enlarged to the size of a $3\frac{1}{2}$ to 4 months' gravidity. A tentative diagnosis of submucous degenerating fibroids was made with sarcoma or carcinoma to be excluded.



Fig. 1.—Roentgenogram showing fluid level with superimposed air in the uterine cavity.

On admission the temperature was 102° F., hemoglobin 57 per cent, white blood count 12,000, with 82 per cent polymorphonuclear leucocytes. Stools were negative for blood. Sedimentation rate over two hours. X-ray of the abdomen (Fig. 1) showed a large mass in the pelvis which extended to the level of the sacral promontory within which there was a fluid level and gas.

Temperature during the first week ranged between 99° and 103.6° F. On July 29, 1942, a vaginal hysterotomy was performed and the uterine cavity was explored. The uterus was found to contain a sessile ragged mass arising from the fundus by a broad base. Because of the extent of the mass, further surgical intervention was deemed inadvisable. A piece of tissue was removed for study. Pathological report revealed "a small fragment of adenocarcinoma with areas of marked spindle cell anaplasia." Following this procedure, the patient was treated with sulfa-

thiazole, but temperature continued to fluctuate between 99° and 103.2° F. Uterine culture taken on July 31, 1942, grew an anaerobic *streptococcus Schottmülleri* and an aerobic enterococcus. On August 8, the uterine cavity was again sounded from below. The sound was passed through the mass and struck a large loculation of pus which apparently was trapped above the tumor. The uterine cavity was irrigated with a 1% emulsion of gramicidin. Clinically the patient improved after this procedure and temperature fluctuated between 98° and 100° F. for several days. The temperature again rose and the uterine cavity was again explored per vaginam on August 22, and another pocket of pus was opened and evacuated. The temperature again fell and uterine culture grew *streptococcus Schottmülleri*. Postoperatively the uterine cavity was irrigated through an indwelling mushroom tube and the patient was treated with sulfonamides, transfusions and deep radiotherapy in an attempt to control the local infection so as to permit surgical extirpation of the infected malignant uterus.

Despite this regime the patient's condition progressively followed a downhill course. It was finally decided that hysterectomy offered the only possibility of bringing this problem to a satisfactory solution, despite the poor condition of the patient who was confused, semicomatose, debilitated and running a septic course. Accordingly, on September 30, 1942, after approximately two months of conservative hospital therapy, a total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus was symmetrically enlarged to the size of a six months' gravidity. The serosa was smooth. The uterus was soft, and its attachments to the parametria were considerably thickened by a boggy indurated process. The tubes and ovaries appeared normal. Pathological report revealed "huge necrotizing rhabdomyosarcoma of the uterus (glandular structures simulating adenocarcinoma seen in focal areas but no cartilage or other teratomatous elements found). Adnexa not involved by tumor."

Following the operation, the patient lapsed into a state of hypothermia. Her temperature remained at about 97° F. for ten days. During this period, she was given numerous transfusions. About two weeks after operation, the patient began to have swinging fever, temperature to 104° F. or 105° F. once or twice daily. She was acutely ill, semicomatose, in *extremis*. There was left costovertebral angle tenderness and pus in the urine. Both urine and blood cultures were positive for *B. pyocyaneus*. Intravenous sulfathiazole and repeated transfusions were administered and the temperature soon fell to normal and the patient slowly recovered. Patient now responded to supportive therapy and gradually gained in strength. She was finally discharged on the sixteenth week of her hospital stay. At discharge her hemoglobin was 70 per cent, she was ambulatory and pelvic examination failed to reveal any local evidence of recurrence of the disease.

At follow-up, 7 months after operation, the patient was ambulatory, carrying on her household duties and showing no evidence of recurrence of the lesion.

Gross Pathology.—The specimen consisted of a uterus and adnexa. It was large, bulky and had a smooth serosa. When opened it measured approximately 20 cm. in length and 14 cm. across. Both tubes and ovaries appeared normal.

The entire lumen was filled by a bulky, soft, greenish, necrotic tissue which was markedly foul smelling. The tumor sprang from the uterine

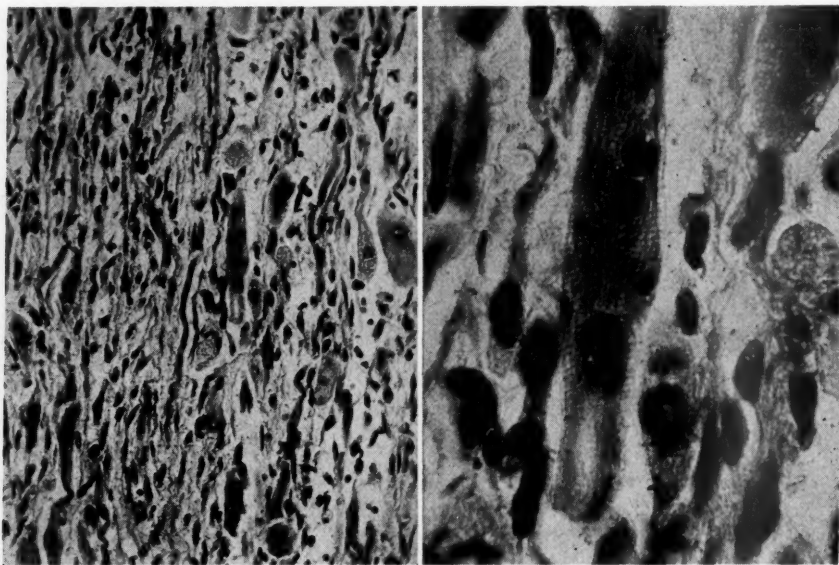
wall, but its growth was almost entirely into the lumen, the serosa remaining smooth and uninvolved. There were several small, firm nodules, approximately one-half cm. in diameter within the uterine wall. They were covered by the necrotic tumor.

Most of the tumor was necrotic and very friable. However, some of the deeper, better preserved portions showed white, smooth, cellular tissue which was fairly soft in consistency.

Microscopic Pathology.—The better preserved areas show marked cellular pleomorphism, but large elongated cells predominate. The picture is one of interlacing cells, running in all directions. There are many bulky, elongated cigar-shaped cells, others are spindle-shaped.

The cytoplasm is abundant and acidophilic in most of the cells and cross striations are frequently seen in the larger cells. The nuclei are either single or multiple and are rich in chromatin, which has a coarse granular appearance. There are many mitotic figures. Some areas reveal marked vascularity and there are many necrotic zones with leucocytic infiltrations. (Fig. 2, A and B.)

Although glandular areas characteristic of adenocarcinoma are seen, these are overshadowed by the predominant picture of rhabdomyosarcoma.



A.

B.

Fig. 2.—A. Low power photomicrograph, showing general cellular topography.
B. High power photomicrograph, showing cross striations.

Discussion

This case is extremely unusual, both because of the rarity of the pathologic lesion and the remarkable clinical course. Many microscopic sections were studied to determine the pathologic diagnosis. Of mesodermal origin, only striated muscle cells were found. On the basis of these findings, one would be justified in considering this a pure rhabdo-

myosarcoma with adenocarcinoma. Nevertheless, there is always the possibility that some unseen fragments of other types of mesodermal tissue were present but not found, since it is almost an impossibility to take serial sections of an entire uterus. Ewing¹⁰ states that the overgrowth of one element in an embryonal teratoma produces a malignant tumor of nearly uniform type, for an important principle of the growth of teratomas is the tendency of one element, either adult or embryonal, to overgrow and suppress the others.

As regards the rarity of diagnosis of rhabdomyosarcoma of the uterus, Lochrane¹¹ believes the scarcity of cases of this condition is due to the fact that special stains are necessary to detect striations, and therefore perhaps many have been missed.

Ewing and Herxheimer¹⁰ have attempted to explain the coexistence of carcinoma with sarcoma by several theories:

(a) Each tumor may develop independently of the other, at the same time, possibly as a result of the same cause acting on different tissues.

(b) Proliferation of the epithelium adjacent to a pre-existing sarcoma may occur, possibly as a result of irritation or stimulation. This may occur at the base of a pre-existing sarcoma, or at a point where a submucous or mural sarcoma meets the epithelial layer.

(c) The stroma of a carcinoma, either due to irritation, stimulation or some other cause, may undergo sarcomatous change (Herxheimer).

(d) Carcinomatous changes may occur in glands of a sarcomatous polyp.

Clinically, several points of interest may be noted. The importance of microscopic study of all tissues removed can never be overemphasized. Six months prior to admission this patient had a "polyp" removed. Perhaps had sections been studied at that time operation might have been performed much earlier. The roentgenologic appearance of a fluid level with gas in a uterus is extremely rare. Several possible modes of occurrence present themselves:

1. By mechanical introduction of air or gas into the uterus via the cervical canal and vagina. Such a case was seen by Snow¹² in which a pneumoperitoneum resulted from forceful or incorrect douching.

2. Infection due to an anaerobic gas forming organism.¹³

3. Manipulation per vaginam with a cervix that remains patulous. Negative pressure in the uterus, with the accompanying sucking in of air associated with infection may result in a fluid level with superimposed air in the uterus.

One or several of these factors may have been operating in this case.

The lack of response to chemotherapy and deep x-ray therapy is very significant.

Lastly, the necessity of surgical intervention, despite the appearance of clinical inoperability, must be stressed. The fact that this patient, in the face of all of the clinical objections to surgery, is now alive and a useful member of her family, makes it necessary to stress the importance of not considering a case inoperable until proved so at the operating table, unless there is evidence of distant metastases.

I wish to express my thanks and gratitude to Dr. Samuel H. Geist, for his aid and stimulating interest in the preparation of this work.

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FETAL DYSTOCIA DUE TO NEUROBLASTOMA OF THE ADRENALS WITH METASTASES TO THE LIVER

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ALTHOUGH a number of cases of neuroblastoma of the adrenal with metastases to the liver in newborn infants or those several days old have been reported, only two reports can be found in the literature in which dystocia was caused by the presence of the tumor mass. The case reported by Hagstrom¹ described a breech delivery in which obstructing parts were encountered at the level of the trunk of the child. Digital examination revealed the presence of a huge liver which later proved to be due to the presence of metastatic tumor masses. Portions of the liver had to be removed before delivery could be completed. Askin and Geschickter's case² was that of a full-term fetus in which the abdomen had to be incised and fragments of the enlarged liver removed before the fetus could be delivered.

The apparent rarity of the complication of dystocia of this origin prompts the following report.

Case Report

The mother of the infant was a twenty-five year-old primigravida, who was admitted to the Sinai Hospital with a history of spontaneous rupture of the membranes four hours before admission. Prenatal examination had revealed a normal bony pelvis, whose configuration was such as not to interfere with the normal delivery of an average-sized infant. The antepartum course had been completely uneventful.

After admission to the hospital, contractions of the uterus began only after stimulation with castor oil, quinine, and divided doses of pituitrin intramuscularly. Cervical dilatation progressed slowly and the head of the infant remained high in the pelvis until full dilatation, which occurred twenty-four hours after rupture of the membranes. Soon after full dilatation the head descended to the midpelvic region, but further progress ceased. Approximately one and one-half hours after full dilatation, a midforceps operation was performed and the patient was delivered of a live male child weighing 2,920 grams. No difficulty

had been encountered in delivery of the head, but hard pressure from above had been required to deliver the torso, which appeared to encounter an obstruction. The cause of the difficulty was quite evident after the delivery of the infant, since marked distention of the abdomen, apparently with fluid, was obvious. The child died one hour after delivery.

Gross Necropsy Findings.—The body was that of an apparently normally developed, full-term male child measuring 47 cm. in length. The striking feature was the protuberance of the abdomen and the bulging in both flanks. The peritoneal cavity was found to contain approximately 200 c.c. of bloody fluid. The liver was greatly enlarged and extended to both lateral borders of the abdominal wall. The right lobe extended three fingerbreadths below the costal margin in the right mid-clavicular line; the left lobe was found to extend two fingerbreadths below the costal margin in the left midclavicular line. The parietal peritoneum in the region of the right kidney bulged forward rather

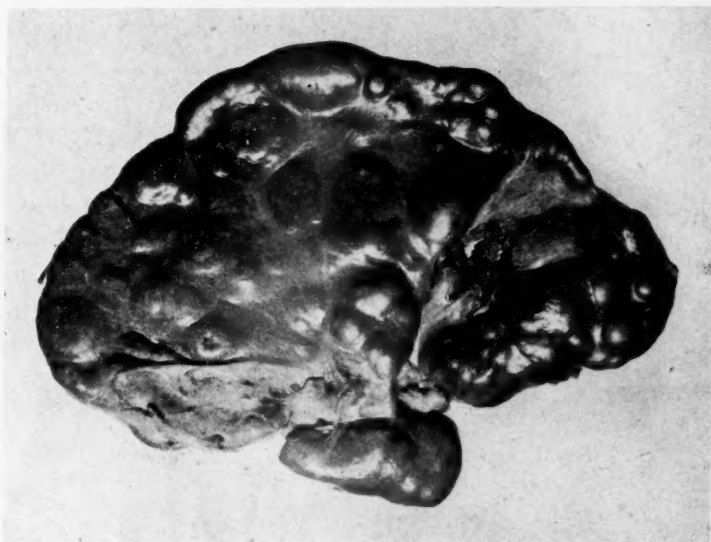


Fig. 1.—Surface of liver showing bosselations produced by metastases.

prominently, forming an oval-shaped mass measuring approximately 10 by 8 by 5 cm. The peritoneum overlying this area had a bluish sheen. Further investigation in this area revealed a deeply hemorrhagic mass measuring 8 by 6 by 3 cm., which occupied the site of the right adrenal and extended downward over the anterior surface of the kidney. It compressed the latter but was distinctly separate from it. It was soft and palpably cystic. Upon sectioning the mass, considerable bloody fluid escaped, revealing the presence of numerous blood clots. In addition, areas of firm grayish-brown and red tissue were also visible. At the upper pole of the mass there was a thin rim of golden-yellow tissue resembling adrenal cortex. The left adrenal was found in its normal position and was relatively normal in shape but proportionately enlarged in all diameters. It measured 4 by 2 by 0.8 cm., weighed 5.8 grams, and felt nodular. The cut surface showed a well developed golden-yellow cortex, which surrounded oval-shaped nodules of grayish-white tissue averaging approximately 1.0 cm. each in diameter.



Fig. 2.—Cut surface of liver showing extensive replacement of liver parenchyma by neoplastic tissue.

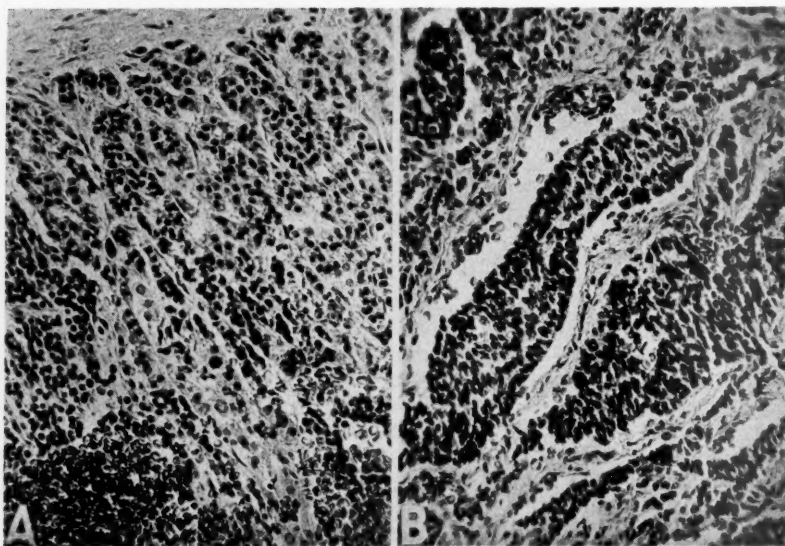


Fig. 3.—A. Section through rim of right adrenal tumor mass showing an area of intact adrenal cortex above an area of invasion by the neoplasm.
B. Section through the tumor mass in the right adrenal showing a typical area.

The liver was huge, weighed 260 grams, and measured 15 by 8 by 4.5 cm. The usual smooth, reddish-brown surface was interrupted practically everywhere by reddish and reddish-gray nodules of varying size, which produced a bosselated appearance (Fig. 1). The nodules varied in size from several millimeters to almost 2 cm. Some of the nodules showed central umbilication. The cut surfaces revealed replacement of most of the liver parenchyma by nodules of grayish-white and brown tumor tissue (Fig. 2).

The heart was normal in size and shape, and, except for the presence of a patent foramen ovale and patent ductus Botallo, was not remarkable.

The other organs showed no gross abnormalities.

Microscopic Examination.—Sections of the right adrenal tumor mass showed large areas of hemorrhage, within which, there were strands and cords of tumor cells, which were round, had a scanty eosinophilic cytoplasm and large round and oval nuclei. Scattered mitoses were seen. In some areas formations suggestive of "rosettes" were seen. The golden-yellow rim of tissue at the upper pole was found to consist of intact adrenal cortex into which scattered strands of tumor tissue were seen to infiltrate (Fig. 3). The sections of the left adrenal showed similar tumor cell masses, which occupied the medullary region, but extended into the cortex, being seen particularly in the interfascicular blood vessels of the latter.

Small nests of tumor cells were found in the interstitial and capsular tissue of the pancreas, in a lymphatic in the wall of the gall bladder, and in blood vessels in the myocardium and cerebrum.

Comment

The pathogenesis and histogenesis of the neoplastic involvement of the adrenals and liver will not be discussed, inasmuch as numerous erudite presentations are already present in the literature.²⁻⁷ The probable mechanism effective in producing dystocia is, on the other hand, of pertinent interest.

Just as in the cases previously cited,¹⁻² the liver in this case was greatly enlarged. But in addition, a bloody effusion was present in the peritoneal cavity in this infant. This certainly contributed to the difficulty of passage of the fetus through the birth canal. The presence of the fluid can be accounted for on the basis of peritoneal irritation by the tumor masses present in the liver.

Although hemorrhagic degeneration in a neuroblastoma has been encountered quite frequently, it is enticing to use the presence of hemorrhage in this case to explain the rapid demise of the infant following delivery. It is possible, and even probable, that very little hemorrhagic infiltration was present in the tumor mass of the right adrenal prior to the onset of labor. This appears to be confirmed by the evident recent nature of the blood clot found in the tumor mass. Therefore, the following evolution of events is offered as being quite likely. With the onset of labor the head passed through the lower uterine segment with ease. However, when the abdomen approached this region, the muscular wall of the uterus failed to dilate sufficiently to accommodate the unusual width, thus forming a constricting band. Therefore, increased pressure was exerted upon the abdomen of the fetus. Inasmuch as the liver was huge, fluid was present in the abdomen and the ribs at this age are quite supple, the constricting force would be transmitted by the above tissues and fluid to the soft tumor mass in the right

adrenal region. Ultimately a crushing pressure would be exerted and then hemorrhage would occur into the disrupted tissue of the tumor mass. Accordingly, as the left adrenal cortex was partly invaded by tumor tissue and only little of the cortex of the right adrenal remained intact, one might blame death upon the shock concomitant with sudden interruption of a sufficient supply of adrenal cortical hormone to maintain the vis a tergo.

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RECURRENT PLACENTA PREVIA

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THE incidence of placenta previa varies from 1:150, as reported by the Committee on Prenatal Maternal Care of the White House Conference, to 1:200 to 1:1,500 as noted by various authors.¹ However, a review of the literature reveals that only nine cases of recurrent placenta previa in successive pregnancies,³⁻⁷ and one in nonsuccessive pregnancies⁸ have been reported. More cases of this type have undoubtedly been observed but not reported, for De Lee¹ and Rivett,² in discussing recurrent placenta previa, speak of a greater than reported frequency. A much larger number of cases in successive pregnancies should be expected in considering the incidence and the predisposing factors of placenta previa. However, this low incidence is apparently due to a failure to report cases and to a few principles of prophylaxis, which may also be of avail in preventing the abnormality. I desire to present another case of recurrent placenta previa in successive pregnancies.

Case Report

Mrs. A. C., aged 19, in the thirty-second week of her first pregnancy, entered the University Hospital at 9:45 P.M. on May 7, 1941, because of sudden, painless vaginal bleeding. The estimated loss of blood was 300 c.c. The prenatal period, as observed in our clinic, was within normal limits. Examination revealed a white female, who had moderate vaginal bleeding and who was not in labor. Her blood pressure was 130/80 and the pulse rate was 100. The uterus had a one-plus tone, was slightly tender in the lower segment area, and measured 28 cm. above the symphysis pubis. A single fetus lay in the L.O.P. position with a fetal heart rate of 140/minute. There was no edema present. On a lateral film of the abdomen, a 32 weeks' fetus was seen in cephalic position, but the placenta was not definitely visualized. Blood count and urine examinations were within normal limits. A diagnosis of placenta previa was made and therapy was instituted. This included blood matching and transfusion which was later followed by sterile vaginal

examination, rupture of the membranes, and application of a tight abdominal binder. Onset of labor was at 10:15 P.M., and after the loss of an additional 200 c.c. of blood, the membranes were ruptured artificially at 12:30 A.M. No placental tissue was felt at the os which was found to be dilated 3 cm. and slightly effaced. After the membranes were artificially ruptured, the fetal head descended immediately and the bleeding stopped. The patient completed a 13-hour labor, spontaneously delivering a three-pound male infant which lived. There were signs of a mild endometritis in the postpartum uterus, which was soft, boggy and tender. The placenta and fetal sac were examined by a water distension method⁹ which showed the sac to have a volume of 1,900 c.c., to be pear-shaped with bulges at the uterine horn areas, to measure 16 cm. from side to side at the widest portion and 24 cm. from the cervical tear to the fundus, and 13 cm. anteroposteriorly. The placenta was 18 by 18 cm. in size, was circular with eccentric implantation of the cord toward the apex, and covered almost all of one anterior or posterior wall. The placenta, moreover, extended downward to within 3 cm. of the cervical rent in the membranes. The diagnosis of placenta previa was further confirmed by the presence of old clotted blood on the placenta at the site of the tear in the membranes.

The patient entered the hospital with a term pregnancy eleven months after her previous delivery with a history of sudden, painless vaginal bleeding, an estimated loss of 200 c.c. of blood. She was not in labor and had no symptoms or signs of toxemia. The soft fundus uteri was 30 cm. above the symphysis pubis. The blood pressure was 130/80 and the pulse rate was 80/minute. A single floating fetus with a heart rate of 135/minute lay in the L.O.P. position. The diagnosis of placenta previa was made again. Blood matching was done, and a sterile vaginal examination failed to reveal placental tissue over the cervical os which was found to be 2 cm. dilated and uneffaced. After the membranes were ruptured, the head descended and the bleeding stopped. Labor followed shortly and a living six-pound eleven-ounce male was delivered 3 hours later. The mother had a normal puerperium. The amniotic sac was distended by 3,400 c.c. of water, and measured 28 cm. longitudinally and 18 cm. laterally. The edge of the sac opening was 1 cm. from the margin of the lowest portion of the placenta, which apparently extended nearly to the internal os. The placenta at this point was infiltrated with old blood clots. The placenta weighed 320 grams, was oval with a longitudinal diameter of 20 cm. and a lateral diameter of 15 cm. It probably lay on the anterior wall of the uterus and slightly to the left side. The cord was 40 cm. long and almost centrally inserted into the placenta. There was a white infarct, 4 cm. in diameter, which extended from the fetal to the maternal surface, and was located about one and one-half cm. above the lower edge of the placenta.

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CLINICAL EFFECTS OF THE SYNTHETIC ESTROGEN, HEXESTROL

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AT THE Philadelphia General Hospital, the gynecology department is constantly faced with the problem of securing an effective estrogenic substance with which to combat the complaints of patients following supravaginal hysterectomy and bilateral salpingo-oophorectomy. This radical procedure is often necessary in young, colored women where chronic advanced pelvic inflammatory disease forces the gynecologist to do castrating surgery, resulting in severe menopausal complaints.

An estrogenic substance to be used in this type of work has to meet certain requirements: it should have a high estrogenic activity if given orally; its action should be prolonged in order to eliminate the necessity of frequent repetition of courses of treatment; it should be nontoxic and thus not cause untoward side reactions; and finally it should be comparatively inexpensive.

It is obvious that the natural estrogens and their derivatives cannot be used for this purpose as they are too expensive and not potent enough when administered orally. We first tried stilbestrol, which has most of the prerequisites mentioned above and which is disappointing in only one way: the frequency of nausea and vomiting. In cases followed by one of us, R. C. M., the frequency of side reactions necessitated a reversion to an oral form of natural estrogen which was not sufficiently potent to control symptoms without the addition of parenteral estrogens. The patients who were somewhat neurasthenic and were warned of the side reactions of nausea and vomiting promptly developed them after the suggestion of its occurrence was made.

We then selected another synthetic estrogen,* hexestrol, for our clinical trials as this material, to judge from what is known about it, seems to come closest to our particular needs.

So far there are only three reports on clinical work with hexestrol.†

Bishop,¹ and his collaborators, made comparative studies on the action of both stilbestrol and hexestrol in relation to the menopausal syndrome, atrophic conditions of the vagina, amenorrhea, dysmenorrhea and checking lactation.

*We are here using the term "synthetic estrogen" to designate substances made synthetically and not having the phenanthrene nucleus as found in natural estrogens. Thus, we are even excluding the natural estrogens when they are obtained by synthetic methods as is now usually the case.

†Two articles have appeared since this present report was prepared, each recommending approximately the same dosage we have found effective.

This work was carried out in England and recently two series on clinical trials of hexestrol have been reported in the United States. It is the purpose of this paper to present a preliminary report of the clinical effects observed in a series of cases with surgical menopause. A subsequent report will be made concerning the use of hexestrol in normal menopause and checking of lactation.

With a number of such patients available, under reasonably well controlled conditions, it was decided to undertake the evaluation of hexestrol therapy in caring for the surgically castrate woman. Seventy-four of these patients were selected for study but it was ultimately necessary to eliminate thirty-two of the group because of their poor cooperation. Wherever possible the treatment was initiated before the onset of menopausal symptoms as a more efficient symptomatic control was expected thereby. In this connection it is interesting to note that Schneider⁴ administered estrogen preoperatively to twenty-one women in whom an artificial menopause was surgically induced. Immediate reinstitution of the same dosage postoperatively resulted in maintenance of freedom from previous symptoms and in a greatly improved convalescence.

Particular attention was paid to the control of symptoms by questioning the patients relative to frequency of hot flushes, headache, nervousness, insomnia, desire for coitus, and as to any side reactions which may have been due to the drug. Four white and thirty-eight colored patients are represented among the forty-two studied. They ranged in age from eighteen to fifty-four years. The women had all been subjected to at least bilateral salpingo-oophorectomy and the majority had had either supravaginal or total hysterectomy performed. The dosage of hexestrol was varied from 2.0 to 6.0 mg. daily with an average daily dose of 3.5 mg.

An analysis of the results reveals that five patients showed no control of hot flushes at any time; four of these patients however lapsed in treatment after averaging seven weeks' treatment and the fifth had only been followed for six weeks at the time this report was prepared, and four patients had no hot flushes at all. Of the remaining thirty-three, twenty showed partial control with seven lapses in treatment, and thirteen complete control of hot flushes with no lapses in treatment. The accompanying headache was uncontrolled in twelve cases, eight lapsed in treatment and six additional cases did not have the symptom. The remaining twenty-four cases showed partial or complete control, only one of the latter lapsed in treatment. Insomnia was absent in eighteen cases and uncontrolled in seven, five lapsed in treatment. In the remaining seventeen cases it was partially (one lapsed) or completely controlled (two lapsed). Fifteen women showed no desire for coitus and the remaining twenty-seven had some or complete return of sexual desire.

At the time this study was begun February, 1941, no adequate dosage was known, and since the previous work done with the drug had shown that the largest dosage used for any length of time was 2.0 mg. daily,

we increased the dosage cautiously. Early in the work it became evident that this dose was inadequate and increases in dosage were made on the scale of 2.0 mg. daily. In four cases the dosage was elevated to 8.0 mg. daily without any appreciable change. In only one case was any side reaction noted and this only in the form of nausea, which began when the drug was instituted and continued throughout the course of treatment. No vomiting was noted at any time.

Although no concomitant series of cases was run using stilbestrol as the estrogenic substance, it is obvious that hexestrol requires heavier dosage than stilbestrol. This statement is based on previous personal experience (R C M) with stilbestrol where 1.0 mg. daily is an adequate maintenance dose. If the treatment is begun on the 6.0 mg. daily dosage of hexestrol, control of symptoms is usually secured in from eighteen to twenty weeks, these figures conform with those cases treated with stilbestrol. This factor is not eliminated but the patient is made comfortable while passing through this period.

An explanation of the final result in the cases is enlightening. In the twelve cases which spontaneously lapsed treatment, all but five were under control and none of these has returned as a recurrence. From a total of nineteen cases discharged asymptomatic, only two have returned with a recurrence of symptoms. These were immediately placed on maximum dosage and are slowly coming under control again. The cases which have been discharged without recurrence have been observed no less than four months and one case as long as ten months. Those patients who are continuing treatment are doing so because of failure to control symptoms completely or because not enough time has elapsed for effective control to make its appearance. In one case only bilateral salpingo-oophorectomy was done and the uterus was allowed to remain; under hexestrol therapy this patient maintains a regular menstrual cycle, anovulatory in type with associated hypomenorrhea.

Several patients suffering from normal menopause are now under treatment and, although the number of cases is insufficient to make an adequate comparison with the surgical menopause, we are led to believe that hexestrol will be effective in controlling this type patient. The patients already show a definite return to a more normal menstrual cycle and control of symptoms. Because of the neurotic element of the normal menopause it is apparent that the correct evaluation of control will be more difficult. The surgically castrate woman has not had the opportunity to develop this element and her control is more easily evaluated. The actual point at which it will be feasible to discharge the normal menopause case will be more difficult to determine and it is expected that recurrence will be more frequent.

Proper study of the vaginal smear, as a method of control, has not been complete in this investigation because of the inability to secure technical aid. This factor is being remedied and the complete report will appear

in a later paper where we shall also report on the value of the drug in other estrogenic deficiency states.

In view of the fact that esters of estrogenic substance often show certain advantages, especially a more prolonged and regulated action, in comparison to the unesterified mother compounds, some preliminary tests were made with hexestryl dibenzoate. This substance is oil soluble, and is reported to be less potent than hexestrol itself, Forman.³ When, in the course of this study, hexestryl dibenzoate tablets, each containing 2.54 mg. of the ester, which amount is chemically equivalent to 2 mg. hexestrol, were substituted for hexestrol tablets, no change in efficiency was observed and no untoward side reactions occurred. The trial of this substance is being continued in the study of the normal menopause cases.

Summary

1. The synthetic estrogen "hexestrol" has been given a preliminary clinical trial.
2. Hexestrol is actively potent in the control of the menopausal symptoms of the surgically castrate woman.
3. A threshold dose has been established at 6.0 mg. daily, which may be given over long periods without producing serious side reactions. Untoward side reactions are so infrequent as to be considered negligible.
4. Hexestrol having this advantage over stilbestrol and, like stilbestrol, being much cheaper than the natural estrogens, and effective when administered orally, it should be submitted to further extensive clinical tests of its value in the treatment of the normal menopause.

The hexestrol preparations used in this study were generously supplied by Jovan Laboratories, Inc., New York, N. Y.

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VULVOVAGINAL MYCOSIS

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THE presence of fungi in the mucous membrane lined cavities of the body has been determined by Benham and Hopkins¹ and Todd.⁵ The disturbances produced by pathogenic fungi in the vagina have been studied by Plass and his co-workers⁶ and Hesseltine.²⁻⁴

The symptoms and signs of mycotic vulvovaginitis vary considerably. The usual complaints are itching and burning of the vulva and vagina, and burning on urination, with or without vaginal discharge. Characteristically the itching is worse during the premenstrual period. The clinical picture has been described in detail by Minnich⁵ and Plass.^{6, 7}

The diagnosis should be made by combined clinical and bacteriologic examinations. Bacteriologic findings in a series of one hundred private patients examined routinely during the last trimester of pregnancy are shown in Table I.

TABLE I

1. PATIENTS NOT VOLUNTARILY COMPLAINING OF VAGINAL AND/OR URETHRAL DISCHARGE OR IRRITATION		96
Monilia	5	
Trichomonas	8	
Monilia and Trichomonas	2	
2. PATIENTS VOLUNTARILY COMPLAINING OF VAGINAL AND/OR URETHRAL DISCHARGE OR IRRITATION		4
Monilia	2	
Trichomonas	1	
Monilia and Trichomonas	1	

One hundred twenty-eight nonpregnant patients complaining of vaginal and/or vulval discharge or irritation were studied in a similar manner with results as indicated in Table II.

TABLE II

1. Monilia	25
2. Trichomonas	97
3. Monilia and Trichomonas	6

The treatment of vulvovaginal mycosis has not been entirely satisfactory in the past. Many agents have been used, the most common one being gentian violet, one or two per cent, in aqueous or alcoholic solution, combined with alkaline douches. This treatment not only gives unsatisfactory results but is unpleasant for both patient and physician. Gentian violet in alcoholic solution gives better results than when in aqueous solution, but in addition to being painful, violent tissue reactions occasionally are encountered in sensitive patients.

Dissatisfied with this form of treatment, Minnich⁵ advocated the following preparation:

Thymol	0.2 per cent
Sodium lauryl sulfonate	3.0 per cent
Eucalyptol	0.1 per cent
Menthol	0.1 per cent
Oil of Wintergreen	0.1 per cent
Sodium perborate	q.s.

The essential ingredients of the powder are thymol, sodium lauryl sulfonate and sodium perborate. It is evident that the percentage of thymol is smaller than one would think necessary to prove fungicidal. However, the action of this drug seems to be enhanced by the other materials contained in the powder, especially sodium perborate. Lowering of surface tension by sodium lauryl sulfonate also plays an important part in producing fungicidal activity. The role of the aromatic oils has not been adequately studied, but it is possible that any or all of these might be eliminated from the formula except for their pleasant odor.

The thymol content of the mixture can be varied if necessary to suit the sensitivity of the patient. However, Minnich⁵ points out that if the thymol content is more than 0.5 per cent, tissue reactions similar to those produced by gentian violet in alcoholic solution may be induced.

He suggests cleansing both vagina and vulva, with particular attention to the clitoris, using a ten per cent solution of the powder (one heaping tablespoon to ten ounces of water). This is followed by daily douches using one tablespoon of the powder to one quart of water. Complete relief of symptoms was obtained in fifteen patients treated by this method, the average duration of treatment being from two to three weeks. Two successive negative weekly cultures were suggested as a criterion for cure.

The author has treated eighteen private patients with vaginal and/or vulval irritation, using the powder suggested by Minnich.⁵ All had positive cultures on Sabouraud's medium. All were relatively acute with the exception of two, one of whom had symptoms of eight months' duration, and the other of one year's duration. In both the latter there were marked skin changes resembling chronic atrophic vulvitis, and both had been treated with most of the preparations commonly employed in the management of trichomonas vaginitis. In both, the principal symptom was pruritus vulvae and ani, and roentgen therapy had been given without relief. One patient had a combined infection, with a mycotic vulvitis and a trichomonas vaginitis.

Therapy in the entire group of patients consisted of biweekly or tri-weekly office treatments depending on the severity of the symptoms. Using cotton balls soaked in a ten per cent solution of the powder (one heaping tablespoon of powder to ten ounces of water), the vagina, vulva, clitoris and anal region were cleansed thoroughly. The vagina

was irrigated with the solution, using a vaginal syringe. The patients were also instructed to cleanse these areas twice daily at home with the more dilute solution (one heaping tablespoon of powder to one quart of water), and to use the remainder as a douche after each cleansing. They were cautioned to make sure that the powder was dissolved, and were instructed not to wear pads. Fifteen patients were treated for two weeks, after which time the vulva and vagina appeared normal and symptoms had subsided. Cultures of the secretions of vagina and vulva on Sabouraud's medium were negative for two successive weeks. In the patient with a combined trichomonas and mycotic infection, the vulvitis was treated first and with results similar to those in the above group. Following this, the trichomonas infection was eradicated by suitable measures. The two patients with symptoms of several months' duration were treated in a similar manner, with gradual decrease in frequency of office visits, until all symptoms had cleared, and the appearance of the vulva was normal. At the end of two months, two negative cultures were obtained at weekly intervals. In one of the patients, itching about the vulva persisted until relieved by injection with ninety-five per cent alcohol.

Discussion

An attempt has been made to verify the effectiveness of a treatment for mycotic vulvovaginitis originally described by Minnich. Results were excellent, clinical and bacteriologic proof of cure being obtained in every instance. In spite of the relatively small number of patients included in both series, the uniform success obtained suggests that this procedure should be employed more often. Those individuals who see more than an occasional case of mycotic vulvovaginitis will welcome its simplicity and effectiveness. Individual cases generally^o will respond to the older methods of treatment, but use of the preparation described above will increase the likelihood of cure and will obviate the undesirable features associated with gentian violet. It is probable that this treatment will prove equally efficacious in the hands of the patient without the necessity of office therapy.

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VAGINAL HYSTERECTOMY

Analysis of 305 Consecutive Cases

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DURING the ten-year period from Jan. 1, 1931, to Jan. 1, 1942, one of us (C. H. T.) has performed 582 consecutive abdominal hysterectomies and 305 consecutive vaginal hysterectomies. This study consists of the 305 consecutive patients upon whom a vaginal hysterectomy was performed at Touro Infirmary and Charity Hospital in New Orleans during this ten-year period. Of the entire series of 305 cases, 138 were Touro and 167 Charity Hospital cases. Most of these patients were white; only 10 in the series were Negroes. This definite preponderance of white women can be explained by the fact that the service at Charity Hospital was chiefly white, and that the vaginal approach is used much less frequently in Negroes than the abdominal. The reason for this is that in Negroes obstetric injuries as a rule are not as numerous, the fibroids are usually larger and the incidence of pelvic infections is greater.

The average age for this series was 44.8 years. Table I shows the distribution. The youngest patient was 27, the oldest 74. The greatest number of operations (171) was performed upon patients between the ages of 35 and 50. Although it is most undesirable to perform hysterectomy on women younger than 35, the age of the patient should not be an absolute contraindication in the presence of extensive prolapse and numerous complaints. Seventeen patients were 65 years or older. Here again, when hysterectomy is advisable, the age of the patient need not be weighed too heavily. The ease of the operation, the low morbidity, and the rapidity with which it can be performed, make vaginal hysterectomy the method of choice for such patients. Most of the cases fall in the age group in which obstetric injuries, complicated by menstrual disorders, abnormal vaginal discharges, and cervical carcinomas are the highest. It is this group of patients that form the greater part of gynecologic practice.

In regard to parity and gravidity, it was found that the greatest number of cases occurred in the group between the ages of 35 to 44, and the frequency in decades diminished as the age increased. Twenty-three patients were pregnant more than

TABLE I. AGE DISTRIBUTION

AGE	CASES	AGE	CASES
27-29	2	50-54	34
30-34	36	55-59	21
35-39	68	60-64	14
40-44	58	65-69	14
45-49	55	70-74	3

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TABLE II. CHIEF COMPLAINT

COMPLAINT	TOURO	CHARITY	TOTAL
Increased vaginal bleeding (irregularity also includes postmenopausal, menorrhagia, clots)	74	75	149
Bearing-down sensation (includes sensation of pressure in pelvis)	48	53	101
Lower abdominal pain	15	56	71
Backache	25	41	66
"Falling of womb"	34	20	54
Vaginal discharge	17	7	24
Bladder trouble (includes frequency and incontinence)	16	7	23
Flooding	5	5	10
Dysmenorrhea (including cramps)	6	3	9
Tumors of womb (carcinoma, "swollen womb")	1	2	3
Lacerations	0	2	2

ten times and 9 had never been pregnant. The average parity of the remainder was 2.8. The maximum parity was 19, and the maximum number of children of any one patient was 14. Of the 31 patients more than 59 years of age on whom hysterectomy was performed, 20 had 4 or more pregnancies, and 11 had less than 3. These 11 cases represent 20 per cent of the patients with a chief complaint of "falling of the womb." In most of the patients 60 or more years of age, hysterectomy was performed because of procidentia. This would suggest that previous pregnancies were not a great factor in the pathogenesis of this condition. In fact, 5 women had never been pregnant!

The chief complaints of the entire series of patients are listed in Table II. Almost one-half of the patients had menstrual abnormalities. Flooding is listed separately because it indicates urgency and was usually the sole complaint. It is also interesting to note that "lacerations" and "tumors" were limited to 5 cases, yet two-thirds of the entire series had extensive cervical disease; 7 patients had complete perineal tears (which were repaired at the time of operation) and uterine fibroids were found in 64. Vaginal discharge, other than bloody, was listed as a chief complaint in 24 cases, whereas nearly all admitted an abnormal discharge upon questioning. Of the 228 women with a history of urinary incontinence on coughing, laughing, or straining, only 23 were sufficiently disturbed by such an event to make it a specific complaint. Two-thirds of the cases had pain or a bearing-down sensation, or both, of such severity as to include this symptom as a chief complaint.

TABLE III. GYNECOLOGIC SYMPTOMS

SYMPTOMS	TOURO	CHARITY	TOTAL
Leucorrhea	131	165	296
Pelvic pain	124	162	286
Backache	125	147	272
Urinary symptoms:			
Frequency	119	155	274
Incontinence	96	132	228
Burning	35	63	98
Pain	30	42	72
Constipation	58	92	150
Menstrual abnormality:			
Menorrhagia	72	115	187
Clots	35	97	132
Metrorrhagia	39	59	98
Dysmenorrhea	26	48	74
Postmenopausal bleeding	36	19	55

TABLE IV. FINDINGS ON EXAMINATION

FINDINGS	TOURO	CHARITY	TOTAL
Cystocele	127	166	293
Rectocele	122	158	280
Chronic cervicitis	129	150	279
Lacerated cervix	87	152	239
Size of uterus:			
Normal	22	5	27
Slightly enlarged	8	8	16
Enlarged	88	132	220
Small	17	3	20
Prolapse of uterus:			
1 degree	39	38	77
2 degrees	51	104	155
3 degrees (prolapsed)	43	25	68
Uterine fibroids	35	27	62
Retroversion of uterus	20	21	41
Stricture of cervix	15	9	24
Amputated cervix	5	3	8
Complete tears	1	6	7
Salpingitis:			
Right	0	4	4
Left	0	4	4
Bilateral	0	1	1
Endometriosis	1	2	3
Cystic ovaries	2	1	3
Abdominal mass	0	2	2
Leucoplakia of cervix	0	1	1
Residual urine	0	1	1
Pyometria	0	1	1
Hemorrhoids	1	1	2

The entire list of gynecologic symptoms is given in Table III. It is apparent that a large percentage of these patients were troubled by numerous complaints. Unfortunately, gynecologic pain and menstrual abnormalities overlap considerably so that rigid analysis cannot be made. Likewise, all complaints are included with regard to severity. Whereas 9 patients had dysmenorrhea sufficiently to complain of it primarily, 74 listed dysmenorrhea when questioned. Burning on urination is differentiated from "pain on urination"; the latter refers to vesical tenesmus, whereas the former refers to the "scalding" that chronic cystitis so frequently causes. Almost 50 per cent of these women were constipated! Fifty-five patients had bloody vaginal discharges and frank uterine postmenopausal hemorrhages, whereas there were 88 patients in whom the menopause had been passed without menstrual abnormality. As one would expect, extensive relaxation of the vaginal outlet resulting in cystoceles and rectoceles was found in 95 per cent and 91 per cent of the series, respectively. The incidence of chronic cervicitis was lower probably because of the atrophy found in cases at or beyond the menopause. In 20 cases the uterus was noted as "small" or atrophic. Palpable enlargement of the organ is not a contraindication for the procedure, since enlargement was noted in 77 per cent of this series. Other findings of particular interest are stricture of the cervix due to previous surgical procedures in 24 cases, complete tears of the perineum in 7, and endometriosis in 3.

Medical complications (Table V) occurred in 74 cases, the most frequent of which was hypertension. Diabetes was present in 4, and was responsible for one of the fatalities. A previous surgical procedure was performed 143 times (Table VI), and 74 patients had had previous lower abdominal operations. Although a lower abdominal scar is a natural deterrent when considering the advisability of the vaginal approach, it need not be held as an absolute contraindication. It should also

be noted that suspension of the uterus was performed in 15, and the interposition operation in 2 cases. At this later date, the advisability of temporizing in these women might be questioned. There is no doubt that the subsequent operation was made more difficult as a result.

TABLE V. MEDICAL COMPLICATIONS

COMPLICATIONS	TOURO	CHARITY	TOTAL
Hypertension (150/90 or over)	33	26	59
Hypotension (less than 100/60)	1	1	2
Other heart disease	0	2	2
Positive Wassermann	0	5	5
Diabetes	1	3	4
Severe anemia	0	1	1
Tuberculosis	1	0	1
Total	36	38	74

TABLE VI. PREVIOUS SURGICAL PROCEDURES

SURGICAL PROCEDURE	TOURO	CHARITY	TOTAL
Cervical:			
Plastic (Including amputation, con-ization and dilatation and curettage)	28	15	43
Radium	4	3	7
Perineorrhaphy	11	7	18
Appendectomy	21	12	33
Suspension of uterus	11	4	15
Salpingectomy:			
Right	4	1	5
Left	1	0	1
Bilateral	1	2	3
Oophorectomy (right)	4	0	4
Hernioplasty (umbilical)	1	2	3
Interposition	2	0	2
Ligation of tubes	0	1	1
"Pelvic operation"	0	1	1
Hemorrhoidectomy	0	1	1
Repair of complete tear	0	1	1
Kidney operation	0	1	1
Thyroidectomy	0	1	1
Cesarean section	0	1	1
"Gall bladder"	0	1	1
Pneumolysis	1	0	1
Total	89	54	143

Eighty-seven per cent of the patients had a maximum temperature of 101° F. or less, and 48 per cent, 100° F. The greatest cause of postoperative fever (Table VII) was urinary in origin, and this occurred in 21 per cent of all cases. Before the advent of the sulfonamide drugs, indwelling catheters, lavage, and urotropin were used to control urinary infection. More recently, extensive local manipulations have been reduced to a minimum by the administration of sulfanilamide and sulfathiazole in full therapeutic doses. The use of these drugs has definitely reduced the incidence of postoperative morbidity. An indwelling catheter has been employed in cases in which urinary retention is a complicating factor, but its use is avoided whenever possible. Postoperative bleeding required packing in 4 instances. Peritonitis was clinically diagnosed in 3 patients, one of whom died. Auricular fibrillation occurred but was controlled without ill effect in one case. As in any series of extensive plastic procedures, bladder injuries were sustained by two patients, in one of whom im-

mediate repair was successful. Later, however, the other patient returned, and the vesicovaginal fistula was successfully closed. Severe postoperative shock occurred in one case, resulting in pronounced atelectasis and death. The mortality rate for this series was 0.65 per cent.

Eighty-one per cent of the patients were in the hospital fourteen days or less with the shortest stay eight, and the longest forty-five days. The average hospital stay for the Touro cases was 12.4 days and for the Charity Hospital group fourteen days.

TABLE VII. COMPLICATIONS

COMPLICATION	TOURO	CHARITY	TOTAL
Cystitis (pyelitis, pus in urine)	39	27	66
Pelvic abscess	1	3	4
Postoperative pelvic bleeding	2	2	4
Wound infection	1	2	3
Peritonitis	1	2	3
Deaths	0	2	2
Auricular fibrillation	1	0	1
Cellulitis of buttocks	1	0	1
Bladder injury repaired (no fistula)	1	0	1
Postoperative vesicovaginal fistula	1	0	1
Parotitis	0	1	1
(Transfusion, preoperative)	0	7	7
(Transfusion, postoperative)	0	8	8
Fatal postoperative shock	0	1	1

TABLE VIII. OPERATIVE PROCEDURES IN ADDITION TO VAGINAL HYSTERECTOMY AND PERINEORRHAPHY

PROCEDURE	TOURO	CHARITY	TOTAL
Repair of complete tear	1	6	7
Salpingectomy:			
Right	0	4	4
Left	1	3	4
Bilateral	3	1	4
Hemorrhoidectomy	3	0	3
Bladder opened	0	2	2
Appendectomy	2	0	2

The entire series of patients had much the same preoperative preparation. A large percentage required no particular preparation other than preoperative cleansing douches and sedation. If procidentia was complicated by cervical erosions and ulcerations, bed rest and daily cleansing douches were employed until the ulcerations had clinically improved. It is felt that the cervical lesions increased the frequency of postoperative infections of the peritoneum, wound, and bladder. In an effort to reduce vaginal flora to a minimum, aqueous merthiolate was instilled following preoperative douches. This caused neither irritation nor annoyance to the patient. If polyps or submucous fibroids were protruding through the cervix, these were removed at least two weeks prior to the vaginal hysterectomy. Opening the peritoneum in the presence of infected polyps or degenerating fibroids increases the frequency of postoperative pelvic inflammation.

In all cases with medical complications, such as hypertension, tuberculosis, and diabetes, medical consultations were requested to prevent complications. One death in this series might have been avoided had the diabetic state of the patient been recognized prior to operation. In the presence of severe anemia, preoperative transfusion was given.

An inhalation anesthetic, either ether or gas, alone or combined, was preferred. A spinal anesthetic was employed if inhalation was contraindicated, but a local

anesthetic was used on one occasion in an elderly patient. It is a remarkable coincidence that pneumonia did not occur as a complication, although severe atelectasis did develop with unfortunate consequences in the one case of severe postoperative shock.

There were slight modifications in the technique of vaginal hysterectomy used in this series. Following preliminary preparation of the vagina, a circular incision was made through the mucous membrane around the cervix. From this an incision was then made in the midline to within 2 cm. of the external urethra. The vaginal mucous membrane was reflected laterally, the bladder displaced upward, and the vesicouterine peritoneal fold incised transversely. The pelvis was explored digitally through the opening in the peritoneum. The anterior wall of the uterus was grasped with the tenaculum and delivered into the vagina. At this stage, in cases of fibroids if it was necessary to reduce the uterine mass, myomectomy was performed. The broad ligament structures were clamped, excised, and ligated separately. These structures were brought together separately in the midline and the upper portion of the broad ligament structures including the round ligaments was sutured to the pubovesical fascia. The base of the broad ligaments was sutured together in the midline and the cul-de-sac eliminated. The vesicovaginal fascia was then sutured together in the midline to the united stump of the broad ligament structures. Interrupted sutures of chromic No. 1 were used throughout.

TABLE IX. MICROSCOPIC PATHOLOGY

PATHOLOGY	TOURO	CHARITY	TOTAL
Chronic cervicitis (including erosion, ulceration)	137	0*	137
Leiomyoma	38	26	64
Endometriosis of uterus	11	0	11
Carcinoma of cervix	7	2	9
Chronic salpingitis	0	6	6
Adenocarcinoma of fundus	0	1	1
Adenomyoma	1	2	3
Cystic ovaries	0	2	2
Sarcoma (leiomyosarcoma)	1	0	1
Cystadenoma of ovary	1	0	1
Angiofibroma of cervix	0	1	1

*Not reported.

Perineorrhaphy was performed in practically every case. Additional procedures were performed as required (Table VIII). The duration of operation varied from twenty to eighty minutes, with an average of 47.7 minutes for the Charity group and 43.7 minutes for the Touro patients. The average time has been found to be shorter for cases of complete procidentia than for cases of incomplete prolapse. This fact has broadened the indications for surgical intervention in the elderly female, since it is felt that the frequency of complications generally is directly proportional to the duration of the operation.

The various pathologic conditions reported are enumerated in Table IX. Chronic cervicitis was the most common condition reported by the pathologist. In 10 cases the malignant condition of the uterus was so early that it could only be detected by the pathologist. It is interesting to note that endometriosis was found in 11 of the cases at Touro Infirmary, whereas this condition was not reported in any case at Charity Hospital.

Summary

A detailed analysis of 305 consecutive cases of vaginal hysterectomy with a mortality rate of 0.65 per cent is presented.

Department of Reviews and Abstracts

Selected Abstracts

THE INFLUENCE OF THE HORMONAL STEROIDS ON URINARY TRACT DISTURBANCES ASSOCIATED WITH GYNECOLOGIC DISORDERS

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THERE have been many recent reports on the clinical effects of the steroid hormones on urinary tract disturbances, especially those associated with gynecologic disorders. This led me to review the effect of the hormonal steroids on the urinary system and to consider the therapeutic uses for, and the dangers in the use of the steroid hormones in urinary tract disturbances associated with gynecologic disorders. The steroid hormones considered are the androgens, the ovarian hormones and desoxycorticosterone acetate.

Differences in kidney structure in the two sexes have been noted. A larger kidney was found in the male than the female guinea pig,¹⁻² mouse³ and rat.⁴ Crabtree⁵ and Selye,⁶ demonstrated that in mice there is a sexual difference in type of Bowman's capsule as well as weight of the kidney. In amphibia there are two types of Malpighian corpuscle in the kidney,⁷ of which one is sexual.⁸ Rugh⁹ reported that he was able to trace the course of spermatozoa through the kidney in the male frog, *Rana pipiens*.

Gonadectomy in male animals has been noted to influence the renal structure. Kidney size and weight decreased after testis extirpation in guinea pigs,¹ mice⁵ and rats.¹⁰⁻¹³ After gonadectomy the kidney size of males decreased much more than that of females, and the kidney weights approximated each other.^{2, 14} After the castration of male mice the Bowman's capsule changed to the female type and the renal weight decreased.^{5, 14} Crabtree⁵ noted that there was also a regeneration of the x-zone or androgenic zone of the adrenal after castration of male mice.

Selye¹⁵ believes that testosterone has a normal physiologic effect on the kidney. The renotropic action of the androgens in the intact animal was noted by Ludden and Kruger¹⁶ and others. Treatment with testosterone propionate was followed by hypertrophy of the "sexual segment" in the kidney of the chameleon (*Anolis carolinensis*).¹⁷ It was demonstrated that treatment with testosterone or its propionate caused marked enlargement of the whole mouse kidney, exaggerated the male characteristic of the kidney in the males and changed the female kidney into the male type.^{6, 18} Histologically, these kidneys were characterized by pronounced hypertrophy of the epithelium of the convoluted tubules and of the epithelial lining of the parietal lamina of Bowman's capsule.⁶ Pfeiffer, et al.¹⁹ noted increased renal weights in young male mice with testosterone and its propionate, and found the latter more active. Testosterone or testosterone propionate caused enlargement of the kidney in the male and female rat also.²⁰ However, the effect was not as marked as in the mouse and was not accompanied by changes in Bowman's capsule. Moreover, testosterone propionate prevented the renal weight decrease action of estradiol.

Korenchevsky and Ross¹⁰ noted the same results and were the first to use the term "nephrotrophic" to describe this androgenic kidney stimulating effect. In immature rats testosterone propionate was also found to produce renal hypertrophy that persisted for a considerable length of time after treatment was discontinued.²¹ Ludden, et al.²² demonstrated that a definite significant increase was produced in the renal weight of male and female rats when testosterone propionate was used. They noted that there was a greater effect in males than in females, and that testosterone propionate appeared to have the most marked effect. When the optimal dose of testosterone propionate was reached, an additional amount produced no further renal enlargement. However, the simultaneous administration of one of the other steroids mentioned produced additional enlargement by an additive effect. They, too, found hypertrophy and perhaps hyperplasia of the convoluted tubules.

The findings in gonadectomized animals treated with the androgens have followed a similar pattern. Renal weight increases in castrated male rats were reported following the administration of androgens.¹⁰⁻¹³ Korenchevsky and Ross¹⁰ and Selye³ described hypertrophy of the kidneys in ovariectomized mice even above that of normal males following the use of androgens. Others²³ reported restoration of the atrophic kidney of the castrated male to or towards normal by the use of androgens. Testosterone restored the sexual characteristics of Bowman's capsule in castrated male mice.¹⁴ Crabtree⁵ compared the findings in male mice after castration with those after castration and treatment with testosterone propionate. She found that the kidney weight which had decreased, increased with hypertrophy of all parts; that Bowman's capsule, which had changed to the female type, returned to the male type; and that the x-zone or androgenic zone of the adrenal, which had regenerated, returned to its former status. Deansely²⁴ found that in young pregnant mice premature degeneration of the androgenic zone of the adrenal accompanied the alteration in amounts and types of endocrines secreted.

It has been inferred by some and shown by others that the increase in parenchymatous renal tissue by the androgens may favorably influence renal function. Testosterone caused an increase in renal tubule activity.²⁵ Diodrast excretion increased as much as 100 per cent after testosterone propionate was given to female dogs. However, neither the glomerular filtration rate nor the renal blood flow was significantly affected. Selye¹⁴ and Longley⁷³ showed that testosterone exerted a protective influence against the kidney damaging effect of sublimate. Others²³ noted that the androgens were able to restore the atrophic kidney to or towards normal. Moreover, renal atrophy, which usually develops subsequent to the hydronephrosis caused by unilateral ligation of the ureter, may be inhibited or delayed by testosterone administration.²⁶ Testosterone propionate considerably increased the compensatory renal hypertrophy following unilateral nephrectomy. Selye²⁰ believes that the kidneys of testosterone treated animals are "functionally superior" to those of non-treated animals in that they are more resistant to nephrotoxic agents. Furthermore, the actions of testosterone esters appear to have no harmful effect on the kidneys except for some pathologic changes in the kidneys of normal rats after very large doses.¹⁰

The findings on the effect of ovariectomy on kidney structure have shown some variations. The kidneys of ovariectomized guinea pigs¹ and mice^{2, 27} were only slightly smaller than those of intact animals. Selye³ found that there was no marked weight decrease in the mouse kidney following ovariectomy. Another group²⁸ saw slight deviations from the normal after ovariectomy in short term experiments. They found, however, that the development of the kidneys became quite subnormal sixty days after spaying. Others found that the size of the kidneys of males decreased much more markedly than that of females after gonadectomy and that the kidney weights approximated each other.^{2, 14, 27}

The results have been variable on the effect of ovarian hormones on the kidney structure of intact animals. One of the earliest workers, Iscovesco,²⁹ used an estrogenic lipid extract of the ovaries and did not notice any change in the size of the kidney. Recently the same results were observed after estradiol benzoate was used in male and female rats.³⁰ In his earlier work Selye^{20, 37} showed that continued therapy with estradiol or diethylstilbestrol caused a marked decrease in kidney weight in the male and female rat. The effect could be counteracted by testosterone propionate, desoxycorticosterone acetate, or progesterone. However, in spite of continued therapy the weight returned to normal limits after a certain time. His later work³¹ showed that estrogens occasionally caused an increase in kidney size. This was always transitory and merely the result of edema. Pfeiffer, et al.¹⁹ demonstrated increased renal weights in young male mice with estradiol benzoate and dipropionate. Others^{10, 22} found that estradiol benzoate, when administered in effective doses, produced a significant increase in renal weights of male and female rats, being greater in the former. The change was produced by the retention of edema fluid in the renal tissues causing the enlargement and increased weight. Progesterone also caused a marked increase in renal weight in male and female rats and mice.^{20, 37} Neither the progesterone nor the estrogens influenced the development of the renal lesions which were produced by the partial occlusion of the aorta proximal to the renal arteries.³²

Slight, if any, kidney weight changes were found following the treatment of castrated males with various estrogens.³³ However, estradiol benzoate caused an increase in kidney weight in ovariectomized rats.^{30, 34} Salvini⁷⁶ noted that in the rabbit the kidney damage, which was caused by certain doses of uranium nitrate, was much greater in ovariectomized than in normal animals. After ovariectomy, estrin exerted a protective influence on the kidneys against uranium nitrate.

The estrogens have been shown to have pathologic effects on the kidney. In 1927, degenerative changes were observed in the kidneys of intact rats following the use of follicular fluid and crude ovarian extracts.³⁵ Recently green granules were demonstrated in the tubular epithelium of the kidney after the administrations of diethylstilbestrol to the intact animal.³⁶ The granules were probably the result of the icterus caused by the drug. More recent investigators¹⁰ found that certain doses of estrogens in ovariectomized and intact rats produced peculiar cystlike degenerative changes in the kidneys. These were mostly confined to the boundary layers of the cortex and medulla. Others³⁸⁻⁴⁰ found that natural estrogens and diethylstilbestrol produced a distension of the ureters and resultant hydronephrosis in the intact animal.

The findings on the effect of adrenalectomy on the kidney structure are in variance. Early investigators⁴¹ in 1916, found that adrenalectomy had no effect on the kidney of the cat. However, diuretics given to the cats caused the appearance of degenerative changes. Later, others⁴²⁻⁴⁵ observed degenerative changes in the kidneys of adrenalectomized cats and rabbits. One observer described the changes as a "lipoid nephrosis." More recent work,⁴⁶ however, failed to reveal any characteristic renal lesions in rats following adrenalectomy.

Desoxycorticosterone acetate increased the renal weight of normal male and female rats and prevented the renal weight decrease action of α -estradiol.²⁰ Ludden and his co-workers²² also demonstrated this and noted that the action was greater in males than in females. When given with testosterone propionate, there was an additive effect. The increase was due to hypertrophy and possible hyperplasia of the convoluted tubules. Desoxycorticosterone acetate had a protective effect in experimental uremia after complete nephrectomy.⁴⁷⁻⁴⁹ After complete nephrectomy was done, the survival time was prolonged, the clinical signs of uremia were delayed, and the rise in the nonprotein nitrogen content of the blood was inhibited.

Hormonal influence on the ureter was first considered by Hofbauer⁷⁴ in 1928. He found a marked hypertrophy and hyperplasia of the musculature and connective tissue of the ureteral sheath of the lowest part of the pelvic portion of the ureter in the second trimester of pregnancy. Recently Prather⁵⁰ considered hormonal activity to be responsible for ureteral atony in the first trimester of pregnancy and for other ureteral changes during the remainder of the pregnancy and the post-partum period. Animal experimentation, however, has led to diametrically opposed conclusions regarding the effect of the steroids on the ureter. Payne and Hodes⁵¹ concluded that there was no ureteral dilatation after injections of prolactin, estrin and progesterone in the normally pregnant rabbit. Another group⁵² also found that there were no significant changes in the ureters after injections of steroids in castrated dogs as compared to controls. Schmitz⁵³ noted that the influence of hormones on isolated pig ureters was not constant. However, estrogens and progesterone were found by others to inhibit peristalsis and muscular activity of the dog, pig and cow ureters in vitro.⁵⁴⁻⁵⁷ In intact mice, natural and synthetic estrogenic substances often produced dilatation and distension of the ureters with resultant hydronephrosis.^{30-38, 58} In the treatment of post-partum pyeloureteral dilatations, the results of stilbestrol administration paralleled an untreated group.⁷⁵ The administration of progestin was productive of very slight regression in only one patient, and in some patients it appeared to increase pyeloureteral dilatation.

Although estrogenic substance effects are primarily manifested in the organs directly concerned with reproduction, structures which have their embryologic origin in the same system may also respond.⁷⁶ The effect of estrogens on the bladder and urethra were described by a number of investigators. Lacassagne⁵⁹ described a progressive proliferation, thickening, and budding of the mucosa in the bladders of a few mice injected with estrone. He thought this to be a direct local effect of accumulated estrone in the stagnating urine. Others found distinct thickening and squamous metaplasia with early keratinization of the epithelium of the bladder in estradiol treated cats and estrone treated mice.^{60, 61} A similar effect on the urethra was found. There was also a marked thickening of the muscular wall with an increase in the size of the muscle fibers. This was considered to be a direct effect of the estrogens. It has been shown that one week after the injection of progynon B, the vesical capacity decreased.⁶² However, the average capacity increased two or three weeks after the injection. This latter finding was noted to occur with some frequency along with dilatation of the ureters and resultant hydronephrosis in mice after the long administration of estrogenic substances.⁵⁸ Hydronephrosis was noted in the intact opossum (*Didelphys virginiana* and *Trichosurus vulpecula*) after estrogenic treatment.^{63, 64} However, the investigators believed that the probable factor was extreme cornification of the urethra causing an obstruction.

The effect of the steroids has been found useful clinically in urinary tract disturbances associated with gynecologic conditions. Estrogen deficient post-menopausal women with urinary symptoms (frequency, dysuria, urgency and incontinence), which were refractory to the orthodox treatment, were treated with estrogens.⁶⁵ The achieved relief of symptoms paralleled the estrogenic effect as evidenced by the vaginal smear. The discontinuance of estrogen therapy resulted in the recurrence of the urinary symptoms and the reappearance of estrogen deficiency as evidenced in the smears. The incontinence was believed to be due to an impairment of the bladder sphincter function on a basis of estrogen deficiency. The other urinary symptoms were due to atrophic lesions of the mucous membrane of the urethral meatus. Following treatment with the estrogens, the mucosa became completely epithelized, like the vaginal mucosa, and the symptoms disappeared.

Steinkamm⁶⁶ recently used estradiol benzoate in an effort to control bladder tone after pelvic operations in women. Little success was noted in attempting to control

the frequent postoperative atony of the bladder after various pelvic operations. The treatment gave benefit, however, in another type of urinary difficulty which often confronts the gynecologist. Estradiol benzoate favorably influenced urinary incontinence which frequently occurred after radical procedures as Wertheim's operation. The effect, he thought, might be due to an improvement in the thickness and tone of the tissue surrounding the urethra.

On the basis of animal experiments, Hoffman and Treite⁷⁸ investigated the influence of estrogens on the bladder tone and capacity of climacteric women. Estradiol benzoate in the form of progynon B was used on nineteen carefully chosen patients. After one injection of five milligrams of estradiol benzoate an average decrease of 35 per cent of the bladder capacity was noted in ten patients. In eight patients there were no noticeable changes, while in one patient there was an increase in bladder capacity. The reduction in bladder capacity was noted on the third day and reached its height between the third and fifth days. In three cases the estrogenic influence persisted for twelve days. An increase of the original dose of five milligrams to ten milligrams did not influence the results. On cystoscopic examination they found an increased vascular injection without any signs of inflammatory reaction. No change in bladder capacity could be determined after corpus luteum therapy. By estrogenic therapy they were also able to improve to a definite extent some cases of relative urinary incontinence in older women.

Mocquot and Moucard⁶⁷ were the first to note that functional disorders of micturition of menopausal women could be relieved with testosterone propionate. Recently Greenblatt⁶⁸⁻⁷¹ noted the alleviation of nocturnal frequency in a series of women who were treated with testosterone propionate for various gynecic disorders. Of the twenty-eight women with this syndrome, nineteen had fibromyomata uteri. In the others, there were stigmata of endocrine imbalance as menorrhagia or dysmenorrhea in the premenopausal group and vasomotor disturbances or atrophic vaginitis in the menopausal group. There was no evidence of the presence of cardiovascular-renal disease, anatomic urinary tract defects, genitourinary tract infection, or psychogenic factors. One young surgically castrate female complained of vasomotor disturbances, dysuria, urgency, and marked nocturnal frequency. Amelioration followed therapy with estradiol and progesterone. No consistent results were noted with progesterone therapy. The author believes that patients with nocturia and diurnal distress should receive an ample course of androgens or estrogens if no pathologic basis can be ascertained, or if the syndrome is refractive to orthodox methods of treatment.

The indications seem clear that the possibilities of clinical usefulness of the steroid hormones in influencing the functions of the urinary tract should be adequately explored on the basis of the findings in the experimental animal. Korenchevsky and Ross¹⁰ suggest that androsterone, which has had marked nephrotropic but weak androgenic effects, would be the androgen worthy of the clinical trial. However, another investigator⁴⁸ believes that desoxycorticosterone acetate has the definite advantage over the androgens in certain cases in not exerting a specific effect on the sex organs. It is believed that patients with chronic nephritis in a stationary status would presumably be put in little or no jeopardy by the constant use of testosterone.⁷² Nocturia, frequency, urgency, and incontinence may have a hormonal basis in those that do not have an organic or psychogenic factor present as the cause of these symptoms.⁷⁰ If no organic or psychogenic basis can be found, or if the syndrome is refractive to the ordinary types of therapy, treatment with androgens or estrogens may be tried. The steroids should also be tried in other urinary tract disturbances associated with gynecologic and other disturbances as well as those already reported. They may be of great value in postoperative gynecologic patients with urinary disturbances.

The possible pathologic effects of the steroid hormones on the urinary tract as found in the experimental animal must be kept in mind. Especially must one consider the possibility of dilatation of the ureters with resultant hydronephrosis in humans with the use of estrogens and progesterone in pregnancy. Moreover, a warning was sounded in a recent editorial that the evidence at hand does not justify indiscriminate treatment of albuminuric and other patients with the steroids.⁷²

Summary

Animal experiments have allowed conclusions to be drawn concerning the influence and working mechanism of the steroid hormones on the urinary tract. The series of clinical observations reveal that the steroid hormones are useful in certain urinary disturbances associated with gynecologic disorders. On the basis of the animal experimentations other therapeutic uses may be found for the steroid hormones in urinary tract disturbances associated with gynecologic disorders.

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6501 NORTH EIGHTH STREET

Selected Abstracts

Sterility

Hotchkiss, Robert S.: *The Male Factor in Fertile and Barren Marriage*, New York State J. M. 41: 564, 1941.

Detailed analyses of the semen of 150 men examined for barren marriage are reported.

The volume of ejaculate averaged 3 c.c. in the fertile group and 2.9 c.c. in the barren group. The average grade of motility was poorer in the barren than the fertile group. The spermatozoa count averaged 64,100,000 per c.c. group as compared to 120,630,000 per c.c. in the fertile group.

The average number of spermatozoa in the ejaculates of barren men was 189,470,000 as compared with 346,020,000 in the fertile men. The average number of oval (normal) spermatozoa in the barren group was 84.17 per cent while the fertile averaged 89.8 per cent. Tapering cells (abnormal) were found in a higher average percentage (10.3 per cent) in the barren than in the fertile group (3.6 per cent).

An assay of fecundity should include a consideration of volume, grade of motility, number of spermatozoa, and percentage of abnormal forms.

J. P. GREENHILL.

Weisman, Abner I.: *Necrostermia*, J. Clin. Endocrinol. 1: 188, 1941.

Weisman states that it has recently been shown that spermatozoa can withstand abnormally low temperatures (0° C., freezing; -196° C., liquid nitrogen; and -269° C., liquid helium) and can survive for as long as 36 to 48 hours at ordinary room temperatures (20 to 23° C.). However, death of spermatozoa after ejaculation may be brought about easily and rapidly by faulty methods of collection. Microscopic examination of the killed sperms leads to the diagnosis of total necrostermia, and the patient may be told he is sterile since all his spermatozoa are found dead (immotile).

J. P. GREENHILL.

Ramos, A. Peralta, and Ramos A. G. Peralta: *Indications and Technic of Artificial Sterilization in Pregnant Women*, Prensa méd. argent. 27: 2347, 1940.

A series of 87 sterilization operations performed during pregnancy is reported. Among 72,553 labor cases five sterilization operations were performed early in pregnancy through the vagina and 16 through the abdomen. In 53 cases, sterilization was carried out at the time of cesarean section. The technique employed in all cases except three, consisted of tubal ligation of the tubes with partial resection. There were two failures in this series.

J. P. GREENHILL.

Wilson, William M.: *Sterility as Affected by Endocrine Disturbances*, West. J. Surg. 50: 6, 1942.

No standardized regime of endocrine therapy for sterility exists. A physician may become encouraged and even enthusiastic over the results obtained in a small

series of cases but is prone to lose faith when further experience indicates that the initial results probably were but a matter of coincidence. The author mentions his own experience with gonadotropic principle of mare serum as a recent disappointment of this character. The possible exception is the use of thyroid extracts in sterile women with low basal metabolic rates.

HUGO EHRENFEST.

Caffier, P.: Sterility Due to Tubal Closure at Uterine End, Zentralbl f. Gynäk. 65: 500, 1941.

The author studied histologic sections removed from the tubes of 16 sterile women in whom physical examination of the adnexa revealed nothing unusual. In 25 of the tubes closed at the uterine end the following conditions obtained:

Adenomyosis of tubes	14
Adenomyosis and chronic salpingitis	3
Chronic salpingitis	4
Endometriosis	3
Adenomyosis of tubes and endometriosis	1

In two-thirds of the cases there was a deepening of the mucosa of the tube with hypertrophic muscular reaction. The rest were divided between inflammation with stricture and endometriosis. The importance of radiography in diagnosis is emphasized, especially for preventing unnecessary operations upon the uterus. None in the series were pregnant three years after reconstructive operations, and it is felt that the operative risk is not consonant with the chances of subsequent pregnancy. In the salpingographic picture the cornu of the shadow is said to be sharper in endometriotic obstruction, while in adenomyosis it is more blunt and stubby.

R. J. WEISSMAN.

Hori, H., Kawamoto, K., and Utiho, I.: Supplementary Study of Sterility, Jap. J. Obst. & Gynec. 24: 2, 1941.

The authors made 734 examinations of the semen in 430 patients. They found nonmotile spermatozoa in the vagina as long as 135 hours after coitus. However, in many cases the spermatozoa escaped from the cervix into the vagina, and they were found in the cervix at the same time. The longest period in which nonmotile spermatozoa were found only in the vagina was 38 hours.

The longest period in which motile spermatozoa were found in the vagina was 37 hours, but the longest time in which active spermatozoa were found only in the vagina was 12 hours.

The longest period in which nonmotile sperm were found in the cervix was 27 days and the longest period in which motile sperm were found in the cervix was 30 days.

In 48 of the 237 cases (20.3 per cent) motile sperm were found in the cervix more than three days after sexual intercourse. Hence, if motility is an indication of fertilizing power, it is possible for sperm to fertilize an ovum even three days after coitus.

J. P. GREENHILL.

Rubenstein, Boris B.: The Vaginal Smear—Basal Body Temperature Technic and Its Application to the Study of Functional Sterility in Women, Endocrinology 27: 843, 1940.

The cycle of gonadal function is studied in relation to vaginal smear changes and basal body temperature. The method of collecting the vaginal material is

described in detail. Smears are stained by the Papanicolaou technic with minor modifications and are evaluated chiefly through the characteristics of the epithelial cells although varying amounts of bacteria, leucocytes, erythrocytes, and mucus are given subordinate consideration. A description is given with colored illustrations of eight types of vaginal epithelial cells, the variation of which indicate ovulation and estrone and progesterone function. The vaginal smear picture is described in detail for all phases of the menstrual cycle. Limitations and possible errors of the method are discussed.

Basal temperature curves are obtained through daily rectal or vaginal temperature readings taken under exacting conditions. The interpretation of the temperature curves is discussed and normal, anovulatory, and climacteric cycles are illustrated.

According to the method of study, out of 739 cycles studied in a group of 101 women, 338 cycles were anovulatory, with no patient being exempt from at least one, but the author cautions against the application of this ratio to the general population as the group studied were relatively infertile.

Forty-eight cases of sterility studied through 308 cycles resulting in 32 pregnancies, 11 abortions, and no result in 27 are reported. Four of the cases indicated ovulation during menstruation. Four pregnancies and no failures occurred in this group.

With the vaginal smear-basal body temperature technic the author attempts to locate the time of ovulation, to determine hormone deficiency, and then to influence the cycle or ovulation by means of appropriate therapy.

CLAUDE J. EHRENBURG.

Complications of Pregnancy

Gillam, J. F. E.: Ruptured Aneurysm of the Splenic Artery During Pregnancy, Brit. M. J. 1: 69, 1942.

The author summarizes 84 cases of ruptured aneurysm of the splenic artery in the literature and adds a case of his own. Of these 85 cases, seven occurred during the last trimester of pregnancy.

The difficulty in diagnosis is emphasized, which is increased by the variability and occasional complete lack of symptoms. Most frequently, colicky pain occurs in the left upper quadrant which is characteristically increased by exertion and by change in posture. Shock, of course, is common. Symptoms referable to the gastrointestinal tract, a pulsating tumor mass and a systolic bruit as occasionally seen.

In 27 cases rupture occurred in two stages: an initial hemorrhage into the lesser sac and a second, and usually fatal, hemorrhage which occurs about two weeks later and ruptures into the peritoneal cavity. The author's case was of this type. Acute left upper quadrant pain followed by signs of profound shock occurred several days before the onset of labor at term. Delivery was uneventful and symptoms subsided. The second hemorrhage occurred on the fifteenth postpartum day. Splenectomy, with removal of the aneurysm was done and the patient recovered.

The author is unable to explain the disproportionately frequent association of pregnancy with this condition.

FRED L. ADAIR AND RAYMOND L. YOUNG.

Martin, J. Purdon: Thrombosis in the Superior Longitudinal Sinus Following Childbirth, Brit. M. J. 2: 537, 1941.

The author reviews some of the literature on puerperal thrombosis of the sagittal sinus, and adds three cases of his own.

The diagnosis of sagittal sinus thrombosis has recently become well established. It depends upon signs of increased intracranial pressure and signs of obstruction of the superior cerebral veins. The author feels, however, that many cases are "silent," diagnosis being impossible in our present state of knowledge.

In his search for an explanation of the etiology of sagittal sinus thrombosis in the puerperium, the author has turned to the recent work of Batson. This worker investigated the connections of the pelvic veins by injecting radio-opaque material into the pelvic veins of cadavers. He found that in addition to their known connections with the caval system, the pelvic veins also have free anastomosis with the veins in and around the vertebral canal, so that a pathway was provided for the transmission of the opaque material to the dural sinuses.

Batson further found that when blood flow to or in the inferior vena cava was obstructed by compression, the flow was diverted to the vertebral venous system. He postulated that the same thing would happen during coughing and straining.

Reasoning from these experiments, the author suggests that a fragment of pelvic thrombus in a puerperal patient might easily be carried to the sagittal sinus and there form a nucleus for the formation of a larger clot.

He suggests, therefore, that the parturient woman suspected of having pelvic thrombosis be cautioned against straining, that the abdominal binder be kept loose, and that the patient be kept well propped up in bed.

FRED L. ADAIR AND RAYMOND L. YOUNG.

Prather, G. C., and Sewall, Weston: Recurrent Pyelonephritis, *New England J. Med.* 226: 291, 1942.

In a series of 72 patients a pyelonephritis of pregnancy recurred during subsequent pregnancies in 23 per cent. If the urine becomes sterile during the interval between gestations, the chance of recurrence is less than one in five, if the urine remains infected the chance is about one in two.

There appears no tendency toward hypertension during a subsequent pregnancy as the result of a pyelonephritis of pregnancy.

HUGO EHRENFEST.

Marshak, R. H.: Postpartum Collapse Associated With Abnormalities of the Cardiac Mechanism, With Continuous Electrocardiographic Studies, *Am. Heart J.* 23: 576, 1942.

A 34-year-old white woman with a history of rheumatic fever but no signs of heart disease, is reported to have gone into severe collapse following prophylactic forceps delivery of her second child. Because of extreme tachycardia, a continuous electrocardiogram was taken. This showed a nodal tachycardia with a rate of 215 beats per minute. Eyeball pressure brought about a return of normal rate with extrasystoles. The patient recovered.

L. M. HELLMAN.

Physiology of Pregnancy

Burrows, Harold, MacLeod, Douglass H., and Warren, F. L.: Excretion of Ketosteroids in Human Pregnancy Urine in Relation to the Sex of the Fetus, *Nature (London)* 149: 300, 1942.

The authors state that morning samples of urine, taken from women from eight to twelve weeks pregnant, show different levels of excretion of ketosteroids. These were measured colorimetrically. Twenty women were tested and it was found that

the ketosteroid excretion values could be divided into two groups according to whether the fetuses turned out to be male or female. Fourteen women bearing male fetuses had an average excretion of 26.2 mg. per liter, while 6 bearing female infants had an excretion of 14.2 mg. per liter. The authors state that, while not significantly different, these results are suggestive and that the work should be repeated.

J. M. HELLMAN.

Beruti, Josue A., and Orellana, David: Prediction of Sex According to the Method of Ryoji Itoh, Arch. Clin. obst. y. ginec. "Eliseo Canton" 1: 79, 1942.

The results of 44 attempts to prognosticate the sex of a child using the method of Ryoji Itoh are presented. This method, which its originator claims to have given a perfect score (in 15 cases), is based on the presence or absence of proteolytic enzyme in the pregnant woman's urine. This enzyme which hydrolyzes testicular proteins is supposedly present only if the child is a male. Using this procedure, the predictions in the 44 cases were correct 24 times and incorrect 20 times, approximately a chance distribution. The accuracy of the predictions was not influenced by the age of the subjects nor by the interval between the test and the time of delivery. The authors consider the test valueless.

J. P. GREENHILL.

Westberg, V.: Histidinuria—Quick Method for the Determination of Pregnancy, Acta obst. et gynec. Scandinav. 112: 180, 1941.

Westberg reviews the Kapeller-Adler method of detecting early pregnancy. A series of 1,023 patients were subjected to the detection of the histidine reaction. The author found that this reaction was negative in 6.3 per cent of healthy pregnant women but if the tests were limited to the first three months of pregnancy, only 3.3 per cent showed negative tests. Urine from nonpregnant women and from men gave negative tests in 98.5 per cent. During the puerperium the histidine secretion rapidly decreased. In a comparison of 171 mice and rabbit pregnancy tests, the histidine reaction compared favorably.

J. P. GREENHILL.

Takenaga, S.: The Process of Fertilization in Humans With Special Reference to the Duration of Pregnancy, Jap. J. Med. Sc. Part 1, 94, 1941.

Takenaga reports the occurrence of five pregnancies in the wife of a physician. Carefully examined records of these pregnancies revealed that biologic tests were positive from ten to thirteen days after fertilization. The entrance of posterior lobe hormone into the urine does not occur immediately after fertilization but only after implantation of the egg in the uterus. The duration of pregnancy varied from 262 to 268 days in the five pregnancies. In this particular patient ovulation occurred at irregular times. Thus, pregnancy followed coitus which took place five days after the last day of the last menses, twenty days after this day, twelve days after this day and twenty days after this day, respectively.

J. P. GREENHILL.

Hartman, Carl G.: Non-Effect of Ovariectomy on the 25th Day of Pregnancy in the Rhesus Monkey, Proc. Soc. Exper. Biol. & Med. 48: 221, 1941.

On the twenty-fifth day in the monkey the corpus luteum involutes in every normal pregnancy, assuming a smaller volume and more compact internal structure characteristic of the greater part of pregnancy. On the twenty-fifth day of gesta-

tion ovariectomy was done and the corpus luteum was removed (other ovary previously removed). The monkey went to term and a 440 Gm. female baby was born after a normal gestation of 165 days. It was concluded that in the Rhesus monkey the ovaries are not necessary from the twenty-fifth day of pregnancy on for normal gestation, parturition at term, and post-partum involution of the uterus and lactation.

WILLIAM BERMAN.

Nixon, W. C. W.: Diet in Pregnancy, Brit. M. J. 2: 703, 1941.

The author considers pregnancy a "diet efficiency" test. He has studied the effects of diet in pregnancy in various Oriental countries and feels that when the strain of pregnancy is placed upon a woman suffering from a subclinical dietary deficiency, the deficiency frequently appears as a clinical disease.

While this seems true for all vitamin deficiencies, it is particularly true of avitaminosis B₁. In Chinese patients approaching term, the frequency of beriberi is significantly increased over the frequency of this disease in the general population.

The author has long been impressed with the close relationship between toxemia and vitamin B₁ deficiency. Of 42 cases of eclampsia, 19 (45 per cent) were complicated by avitaminosis B₁. Of the 13 fatal cases in this series, 11 were so complicated. On the basis of this and other work, he believes that there is a positive correlation between the severity of a toxemia and B₁ deficiency.

In an effort to improve maternal welfare, the author makes three recommendations: close dietary supervision of prenatal patients, with trained dietitians available for instruction in the preparation of adequate, low-budget diets; practical instruction in modern dietetics for doctors and nurses; and, improvement in hospital diets.

F. L. ADAIR AND RAYMOND L. YOUNG.

Plotz, E. I.: Histidin Excretion in Urine of Pregnant Women, Zentralbl. f. Gynäk. 65: 309, 1941.

Noting the apparently parallel excretion of histidin and prolan in gravid women, Plotz determined qualitative histidin in urine of 100 pregnant and 119 nonpregnant women by the Kapeller-Adler method, (Klin. Wehnschr., p. 1728, 1936). The reaction was positive in 96 per cent of pregnant women and accuracy was improved in the later months of pregnancy. Seven and five tenths per cent were found to have histidinuria. The reaction disappears eight days post partum and six days post abortum. The author feels that negative findings give a more secure basis for ruling out pregnancy than the same findings in the Aschheim-Zondek test. Failures of the test may be expected in hypophyseal tumors, thyrotoxicosis and in the preclimacteric years.

R. J. WEISSMAN.

Zohn, Benjamin: The Relationship of Maternal Diet to Intrauterine Sensitization, J. Allergy 13: 153, 1942.

Certain experimental studies on animals and some clinical observations have supported a belief that during pregnancy some food sensitivities can be started in the fetus by the diet of the mother.

In a study made on 21 pregnant women, Zohn found that excessive consumption of such foods, as chocolate, milk, egg, strawberry, potato, buckwheat, banana, plum, and peach, had no demonstrable effect on the offspring from a viewpoint of sensitization.

Hence any control of the maternal diet during pregnancy aimed at prevention of intrauterine sensitization does not seem justified.

HUGO EHRENFEST.

Vignes, H.: **Ovarian Rhythm During Pregnancy**, *Rev. franç. de gynéc. et d'obst.* 36: 18, 1941.

The duration of pregnancy is approximately 10 menstrual cycles. There is a mild return of menstruation about a half menstrual cycle after labor and a return of full menstruation about a cycle and a half after delivery. Re-establishment of menstruation after abortion is fairly constant, between one and one and one-half menstrual cycles after the abortion. Spontaneous abortions generally begin during the phase which would have corresponded, if menstruation had continued, with the lutein phase between ovulation and menstruation. Hemorrhages during pregnancy often occur with a periodicity resembling that of menstruation. It is, therefore, not irrational to suppose that ovarian rhythm continues during pregnancy.

J. P. GREENHILL.

Radiation

Kolbow, H.: **Uterus and Vagina in Lateral Roentgenogram**, *Zentralbl. f. Gynäk.* 65: 748, 1941.

The author has found diagnostic value in lateral films taken with the patient standing, after outlining uterine cavity and tubes with iodized oil, and injecting 10 to 20 c.c. into the vagina. When the patient stands most of the oil flows out, but enough remains to outline the vagina satisfactorily. Exposure 0.6-0.8 sec., kv. 95, P 40, 3.3 mm. Al. filter, 120 Ma. The position of the uterus in relation to vaginal axis is clearly demonstrated, and by filling the bladder to varying capacity, the changes in uterine position may be observed. Active contractions of the vaginal wall were seen after administration of pituitrin, during which the posterior wall became shortened and closely applied to the cervix. The author calls attention to the significance of this mechanism for conception, in contrast to the infantile uterus whose portio does not come in full contact with the receptaculum of the sperm. Retroversion and retroflexion are easily diagnosed, and it is clearly shown that the vagina bends midway to take a more posterior direction in its upper portion.

R. J. WEISSMAN.

Hady-Gediz, M. A.: **Radium in Chronic Cervicitis**, *Zentralbl. f. Gynäk.* 65: 633, 1941.

The author discusses the complications of the usual treatments of chronic cervicitis. In his Istanbul clinic he has used radium application of 300 mg. hr. with excellent results in a small series of 12 cases. No untoward effects on menses or fertility have been noted. In this series all cases having more extensive inflammation of uterus or adnexae were not included. A second application of 200 to 250 mg. hr. is given six months later for any residual symptoms, although the author does not state how many of his patients required 2 applications. The vagina is cleansed and mucus cleared from the cervix, which is dilated to take Hegar No. 10. A small gauze tampon is passed to the internal os and the radium, in platinum-iridium containers within a 1.5 mm. brass filter tube is inserted in the cervical canal. The deepest part of the tandem contains 5 mg. of radium, followed by two 10 mg. containers. A 1 mm. rubber capsule may be placed over the whole to give some added filtration effect.

R. J. WEISSMAN.

Ehrhardt, K.: **Fetal Organography—Intraamniotic Thorium Injection**, *Zentralbl. f. Gynäk.* 65: 114, 1941.

The author replaces 8 to 10 c.c. of aspirated amniotic fluid with an equal amount of thorotrast. The colloidal thorium in a four to five months pregnancy becomes

diluted approximately 1:25 and is seen shortly after injection as a diffuse shadow outlining the amniotic sac. In cases of fetal death subsequent films reveal no changes. The living fetus, however, is constantly imbibing amniotic fluid and after an interval of twelve to forty-eight hours the thorium becomes concentrated in the fetal gastrointestinal canal and radiography of the fetus in utero or after delivery reveals all details of the tract. A good concentration of thorium in the lungs brings out their outlines and gives further evidence of intrauterine "respiration." Ehrhardt believes this contrast injection may be useful in cases in which pregnancy is to be terminated shortly as an aid to more exact knowledge of the fetal status, and intrauterine activity.

R. J. WEISSMAN.

Utzuki, A., and Hashidzume, H.: Roentgenologic Delineation of the Fetal Surface in Utero, Zentralbl. f. Gynäk. 65: 194, 1941.

In cases of acute hydramnios and where there was evidence of fetal death or monstrosity, the authors have successfully outlined the fetal surface by injecting 15 c.c. of an organic iodized oil into the amniotic fluid via an abdominal puncture after first drawing off from 1 to 2 liters of fluid. The puncture is made 1 cm. below the umbilicus 3 or 4 cm. lateral to the midline. Three cases are presented with excellent radiographs. Details such as hair, digits, scrotum and penis, eyelids, umbilicus can be seen. Maceration of the skin of a dead fetus is readily determined. There appears to be an affinity between the oil and the fetal skin and vernix. No ill effects upon the mother were noted in the cases cited. The first infant was born dead, spontaneously, the day following the injection. Poly and syndactylia, which were noted on the films, were present, as well as incomplete development of the gastrointestinal tract. In the second case the maceration of the fetus was clearly outlined. Spontaneous delivery of a dead infant occurred three days later. In the third case, with a diagnosis of acute hydramnios the procedure clearly outlined an edematous fetus. The infant was born 18 hours later but died on the following day. This infant had a dextrocardia. Unfortunately autopsy permission was refused. The authors feel the method has great diagnostic potentialities and is possibly harmless to the fetus.

R. J. WEISSMAN.

Breitländer and Heinrichs: Pulmonary Embolism after Iodized Oil Hysterosalpingography, Zentralbl. f. Gynäk. 65: 124, 1941.

The authors present a case of accidental intravenous deposition of iodized oil, with survival of the patient. A 57-year-old woman complaining of bloody vaginal discharge of several months' duration had a mass the size of a child's head palpable on the right of the uterus. A diagnostic curettage was done and as the curette sank to a depth of 17 cm. in the corner occupied by the tumor, iodized oil was injected under radiographic control to determine whether the uterus had been perforated. Films taken eighteen hours later showed iodine shadows in the periuterine veins, ovarian veins and continuing upward. Shortly afterward a chest film showed a fine distribution of the contrast medium through the pulmonary vessels. As the patient showed no ill effects from this accident she was subjected to panhysterectomy five days later. At no time were there any palpatory, percussion or auscultatory changes in the lungs and the patient made an uneventful recovery from her operation. The authors calculate that from 10 to 20 c.c. of the material found its way into the venous system. An incidental observation of physiologic interest is the fact that the movement of venous blood in the pulmonary system takes place in concert with left ventricular systole.

R. J. WEISSMAN.

Eastland, William E.: *The Role of Deep X-ray Therapy in Pruritus Vulvae*, South. M. J. 34: 324, 1941.

The medical literature contains few references to the use of deep x-ray therapy in the treatment of pruritus vulvae. In certain types designated as idiopathic, essential or neurogenic, an exact cause cannot be discovered, and the ordinary therapeutic measures are ineffective; here deep x-radiation has been used to advantage. It is not advisable to employ deep x-ray treatment for the pruritus that accompanies leucoplakia and kraurosis.

There was definite symptomatic improvement in six of the seven patients whose clinical course formed the basis for this report; the seventh patient was given a lighter dose of x-ray, and the amelioration of symptoms was only temporary. The factors in the author's technique are, 200 kv., 20 ma, 50 cm., S.T.D. with a tin-copper-aluminum filter equivalent to 2 mm., of copper. Two hundred r. units is given once a week for three or four weeks.

ARNOLD GOLDBERGER.

Labor—Management and Complications

Nakamura, T.: *The Effect of Lack of Vitamin C Upon Labor*, Jap. J. Obst. & Gynec. 23: 176, June, 1940.

The author found that lack of vitamin C during pregnancy resulted in abortion and the lack of this vitamin during the puerperium interfered with the mechanism of involution of the uterus. Most of the young, born of mothers with vitamin C deficiency, were either stillborn or very frail.

Sala, Silvestre Luis: *Value of Rectal Examination in Obstetrics*, Arch. Clin. obst. y ginec. "Eliseo Cantón" 1: 118, 1942.

Sala classifies available authoritative opinions on this subject and finds that they range from a decided partiality for rectal examinations to a complete denunciation of this method with some intermediate opinions favoring the use of both rectal and vaginal examination according to the circumstances. A survey of the opinions of the heads of the maternity hospitals in various countries made by Sciclounoff in 1935 indicated that 91.99 per cent used rectal examination, but not exclusively, while only 7.99 per cent used it exclusively. It was also shown by this survey that the method was chiefly used in Germany, Switzerland and the United States, and that many obstetricians regarded it as a dangerous procedure. Some of the conclusions of this survey are re-examined in conjunction with an analysis of the author's own data comprising 2,000 cases observed in the clinic since 1939 when rectal examinations were first practiced.

Sciclounoff's survey indicates that 72 per cent of the men questioned did not consider vaginal examination more conducive to puerperal morbidity and mortality than rectal examination. The author's survey of 16 published studies on this matter shows that the majority consider rectal examination more favorable, although generally only slightly more so than vaginal examination. He criticizes the data employed in most of these studies because they are not rigidly selected and offers an analysis of his own carefully selected data. This leads, however, to the same conclusion, that puerperal morbidity is slightly lower with rectal examination (6.9 per cent) than with vaginal examination (9.1 per cent). He adds that the publicized dangers of the latter are exaggerated.

Concerning the diagnostic reliability of the rectal method, even its most vigorous defenders concede an average error of 10 per cent. In the 2,000 cases analyzed by the author, rectal examination led to 28.8 per cent inadequate or erroneous

diagnoses. In 80 cases, diagnosis by rectal examination was checked by subsequent vaginal examination and found to be corrected in 31.2 per cent and incorrect in 68.7 per cent; these were, of course, cases which presented diagnostic difficulties. The author considers the inherent difficulty of the method one reason for the high percentage of errors. The paradoxical finding in these data that the percentage of error increased as the skill and experience of the examiner increased he believes occurs because the most difficult cases are reserved for the most experienced and competent men.

Diagnosis of cervical dilatation by rectal examination was faulty in 9.9 per cent of the cases, but analysis showed that the height of presentation is an important factor, the percentage of error in judging dilatation is greatest when the presentation is high. The magnitude of error in diagnosis is sometimes very great, confusion existing between the fully dilated cervix with intact membranes and the undilated, but completely effaced cervix.

Diagnosis of the condition of the membranes is most difficult by rectal examination. The author found 18.2 per cent of error in such diagnoses and again found that the height of the presentation directly influenced the incidence of error.

Diagnosis of the presentation is generally considered easy by the rectal method although occasional gross errors have been recorded in the literature. The author found 1.2 per cent of error in his data and again the proportion of error was greater the higher the presentation. Errors almost always concerned confusion of breech presentations with cephalic. Only 0.3 per cent of error was found in diagnosing the height of the presentation.

The author concludes that rectal examination entails less puerperal morbidity than vaginal examination, but is at a disadvantage in diagnosis. However, the inadequacy of rectal examination in this respect diminishes to reasonable limits if only the factors of cervical dilatation and height of presentation are concerned, the two determinations generally sufficient for conduct of normal deliveries. Vaginal examination, however, is essential for diagnosis in abnormal or doubtful cases.

J. P. GREENHILL.

Vara, P.: Observations on Early Rising After Gynecologic Operations and Labor, *Acta. obst. et gynec. Scandinav.* 112: 168, 1941.

In the Woman's Clinic at Helsingfors, 4,447 women were allowed out of bed very soon after delivery and 795 women were allowed out of bed early after gynecologic operations. Vara found that the incidence of thrombosis was definitely less in these women than in women who were permitted to remain in bed longer after delivery or operation. Likewise, there was improvement in function of the bowels and bladder, and the period of convalescence was shortened.

J. P. GREENHILL.

Thoms, Herbert: Inversion of the Uterus, *Yale J. Biol. & Med.* 14: 399, 1942.

The author reviews the factors tending to produce inversion of the uterus. He emphasizes again that the chief contributing factor is the mismanagement of the third stage of labor. However, a certain incidence of uterine inversion will occur even in expert hands, so called, spontaneous inversion. The author discusses acute and chronic inversion, and mentions the generally accepted methods of treatment for the latter, with manual replacement from below and laparotomy with traction from above being the most common forms of treatment in acute inversion. Two cases of chronic inversion of the uterus are described.

WILLIAM BERMAN.

Mehta, Chamam Lal: Management of Breech Presentation by External Version and Its Effects on Prematurity and Mortality of Infants, *J. Indian M. A.* 10: 1, 1941.

The author is in agreement with the general literature that the best treatment for breech presentation is external version. External versions were performed from the twenty-sixth week onward. The thirtieth to the thirty-second week is the best time for attempting external version. The authors feel that breech presentation is a cause of prematurity. The incidence of prematurity in this series was 12.63 per cent (using fetal weight of 5 pounds as a sign). The fetal mortality was higher in the premature than in the mature (25 per cent to 8.42 per cent). The author encountered no complications. There has been a considerable fall in the percentage of premature children and fetal mortality as a result of external version.

WILLIAM BERMAN.

Coventry, W. A.: The Management of the Breech, *Journal-Lancet* 62: 1, 1942.

The author is fully in accord with the method of Potter. He points out several cardinal principles in breech delivery, namely (1) the cervix must be completely dilated or dilatable, (2) complete anesthesia, and (3) the perineum must be completely ironed out. After these things have been done the operator can bring down one or both feet, depending upon the ease of operation. The buttocks should be delivered posteriorly. It is advisable to use steady traction with one hand at the baby's ankle. When the umbilicus is reached, a portion of the cord is pulled down and traction continued. The shoulders are delivered anteriorly. The delivery of the head can take time. The head is delivered either by aid of the index finger in the baby's mouth or by Piper forceps if necessary. Traction should never be placed over the baby's shoulders. The author allows fifteen minutes for a simple uncomplicated breech delivery.

WILLIAM BERMAN.

Fleming, John G.: Previous Uterine Infection as a Predisposing Cause for Spontaneous Rupture of the Uterus, *Ohio State Med. J.* 37: 747, 1941.

Two cases of spontaneous rupture of the uterus at term, in patients with a history of previous uterine infection following term delivery and infected induced abortion, respectively, are reported. Similar pathologic changes of the uterine wall, consisting of marked degeneration and atrophy of the muscle cells and extensive replacement of the myometrium by fibrous connective tissue, were found in both cases. Patients with a history of a previous uterine infection, whether following abortion or term parturition, warrant close observation during subsequent pregnancies and deliveries against the increased incidence of serious complications, including spontaneous rupture of the uterus.

J. P. GREENHILL.

Houston, Craig S.: Report of Bagging Cases at Providence Lying-In Hospital, *Rhode Island Med. J.* 23: 207, 1940.

Among 226 cases (1926 to 1938) where a bag was used, 168, or 30 per cent, were in labor more than twelve hours after the bag was inserted. In this connection it is of interest that in six cases a bag was inserted twice, in two cases the bag was expelled without any dilatation, in two cases the bag broke and in four cases it was removed without having accomplished anything after twenty-four hours. This gives a total of 14 cases in which nothing at all was accomplished in way of dilatation by use of bag.

Thus there were 28 cases where there was not sufficient dilatation obtained by bag for delivery and manual dilatation or cesarean section was necessary. This is in addition to the fourteen cases above mentioned where nothing was accomplished by the bag giving a total of 18.6 per cent where the bag did not give very satisfactory results as far as dilatation of the cervix was concerned.

There was a morbidity of 67 or about 30 per cent. This includes ten cases of severe post-partum shock and six cases of severe sepsis. There were eight cases, or 3.5 per cent, of prolapsed cord after the bag was inserted. The fetal mortality was high, 34 cases, or 59.24 per cent.

There was a total maternal mortality of 19 cases, or 8.4 per cent. Ten of these died during the first three years which this study covers.

In analyzing these cases further there were eleven who had eclampsia or severe toxemia out of 96 cases; seven who had a placenta previa or separated placenta out of 92 cases; and one case of pernicious vomiting.

As a result of this study, the author's opinion is that there is a place for the use of the bag in obstetrics, but it must be remembered that there is considerable risk to the mother and an extremely high fetal mortality. It does not seem advisable to attempt bagging unless the cervix is easily dilatable as failures were frequent with a rigid cervix. In the past few years simple rupture of the membranes has replaced use of the bag in cases of marginal placenta previa where the cervix is easily dilatable, while cases of central and partial placenta previa and cases with a rigid cervix are better treated by cesarean section. The author thinks that the use of a bag is seldom indicated to induce labor or to hasten dilatation of the cervix, as the danger of infection is great and failure of the bag to accomplish dilatation is very frequent.

J. P. GREENHILL.

Dr. Fred J. Taussig died at Bar Harbor, Maine, August 21. An extended obituary will appear in an early issue of the JOURNAL.

Item

American Board of Obstetrics and Gynecology, Inc.

A number of changes in Board regulations and requirements became effective at the annual meeting of the Board, May 20, 1943. Several of these changes are designed to broaden the requirements for candidates in Service. Examples are the allowance of a stipulated amount of credit toward special training requirements for men in Service and assigned to general surgical positions, special training allowances on a preceptorship basis for men assigned to obstetric or gynecologic duties in military hospitals and working under the supervision of Diplomates or recognized obstetrician-gynecologists, as well as credit toward the "time in practice" requirement of the Board to be allowed for time in Military Service.

The Board will no longer require a general rotating internship, but will now accept a one-year intern service, although the rotating internship is preferable. Such services must be in institutions approved by the Council on Medical Education and Hospitals of the A. M. A. Lists of such institutions are published regularly in the Educational Number of *The Journal of the A. M. A.*

The privilege of reopening applications by candidates who have been declared ineligible has been extended to two years from date of filing the application, instead of one year.

The Board has ruled temporarily to excuse men in Military Service from the submission of case records at the stipulated examination times, thereby permitting them to proceed without further delay with the Board examinations. This does not obligate the Board, however, to waive the case record requirement for such candidates. Plans have been made to provide similarly for Service men upon their eventual discharge from the Armed Forces, and to permit the greater use of operations done while in residency or in civilian practice before the War.

The next Part I examination of the Board (written paper and submission of case records) will be held on Saturday afternoon, February 12, 1944, at a place convenient to the location of the candidate, whether he be in civilian or military life. Applications must be in the Office of the Secretary by November 15, 1943, ninety days in advance of the examination date. The time and place of the Spring 1944 (Part II) examination will be announced later.

Prospective applicants or candidates in Military Service are urged to obtain from the Office of the Secretary, a copy of the "Record of Professional Assignments for Prospective Applicants for Certification by Specialty Boards" which will be supplied upon request. This record was compiled by the Advisory Board for Medical Specialties and is approved by the offices of the Surgeons-General, having been recommended to the Services in a circular letter, No. 76, from the War Department Army Service Forces, and referred to as the Medical Officers Service Record. These will enable prospective applicants and candidates to keep an accurate record of work done while in Military Service and should be submitted with the candidate's application, so that the Credentials Committee may have this information available in reviewing the application.

Applications and bulletins of detailed information regarding the Board requirements will be sent upon request to the Secretary's Office, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

PAUL TITUS, M.D., Secretary.